STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 179757

TO: Ernst Arnold Location: 4b49 / 4c70 Tuesday, February 28, 2006 Art Unit: 1616 Phone: 571-272-8509 Serial Number: 10 / 524144	From: Jan Delaval Location: Biotech-Chem Library Remsen 1a51 Phone: 571-272-2504 jan.delaval@uspto.gov

Search Notes

FOR OFFICIAL USE ONLY 179757 ACCESS DB # _____

PLEASE PRINT CLEARLY

Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: Ernst Arnold Examiner # : 80868 Date: 02/16/06

Art Unit: 1616 Phone Number: 2-8509 Serial Number: 10/524,144

Location (Bldg/Room#): 4R59MB49 (Mailbox #): 4C70 Results Format Preferred (circle): PAPER DISK

****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Use of Treosulfan and derivatives for treating MS

Inventors (please provide full names): Sass, Gretel

Earliest Priority Date: 08/12/03

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only ***Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.***

Please search:

Treosulfan (treosulphan)

CAS NO: 299-75-2

1,2,3,4-butanetetrol, 1,4-dimethanesulfonate

1) method of treating multiple sclerosis w/ treosulfan

2) method further comprising treosulfan and intereferon and/or glatiramer acetate.

3) Any composition w/ treosulfan and interferon and/or glatiramer acetate.

note: ph ≈ f in the words

please include:

1) busulfan (busulphan)
2) dimethyl busulphan
3) pentasulphan
4) hepsulphan

STIC SEARCH RESULTS FEEDBACK FORM

Biotech-Chem Library

Questions about the scope or the results of the search? Contact ***the searcher or contact***:

Mary Hale, Information Branch Supervisor
22507, Remsen 1d86

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

- *Relevant prior art **not found:***
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

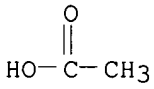
Drop off or send completed forms to STIC/Biotech-Chem Library CM1 – Circ. Desk

```
=> fil reg
FILE 'REGISTRY' ENTERED AT 15:16:21 ON 28 FEB 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   27 FEB 2006  HIGHEST RN 875402-35-0
DICTIONARY FILE UPDATES:  27 FEB 2006  HIGHEST RN 875402-35-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

*********************************************************************
*                                                                   *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                   *
*********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> d l58 ide can tot

L58  ANSWER 1 OF 6  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   147245-92-9  REGISTRY
ED   Entered STN:  28 Apr 1993
CN   L-Glutamic acid, polymer with L-alanine, L-lysine and L-tyrosine, acetate
     (salt) (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   L-Alanine, polymer with L-glutamic acid, L-lysine and L-tyrosine, acetate
     (salt) (9CI)
CN   L-Lysine, polymer with L-alanine, L-glutamic acid and L-tyrosine, acetate
     (salt) (9CI)
CN   L-Tyrosine, polymer with L-alanine, L-glutamic acid and L-lysine, acetate
     (salt) (9CI)
OTHER NAMES:
CN   Cop 1
CN   Cop 1 (polyamide)
CN   Copaxone
CN   Copolymer 1
CN   Glatiramer acetate
CN   L-Glutamic acid peptide with L-alanine, L-lysine and L-tyrosine, acetate
     (salt)
```

FS STEREOSEARCH
MF (C9 H11 N O3 . C6 H14 N2 O2 . C5 H9 N O4 . C3 H7 N O2)x . x C2 H4 O2
CI COM
PCT Polyamide, Polyamide formed, Polyester, Polyester formed
SR World Health Organization (WHO)
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO, CA, CAPLUS, CBNB, CIN, DIOGENES, EMBASE, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PATDPASPC, PHAR, PROMT, PROUSDDR, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

CM 1

CRN 64-19-7
CMF C2 H4 O2



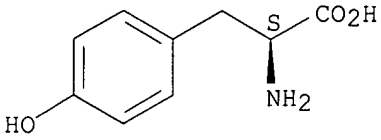
CM 2

CRN 28704-27-0
CMF (C9 H11 N O3 . C6 H14 N2 O2 . C5 H9 N O4 . C3 H7 N O2)x
CCI PMS

CM 3

CRN 60-18-4
CMF C9 H11 N O3

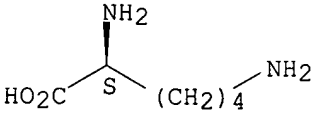
Absolute stereochemistry. Rotation (-).



CM 4

CRN 56-87-1
CMF C6 H14 N2 O2

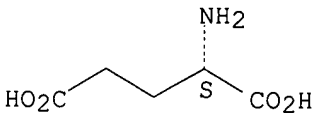
Absolute stereochemistry.



CM 5

CRN 56-86-0
CMF C5 H9 N O4

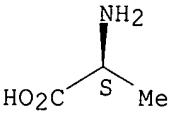
Absolute stereochemistry.



CM 6

CRN 56-41-7
CMF C3 H7 N O2

Absolute stereochemistry. Rotation (+).



311 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
312 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 144:177492

REFERENCE 2: 144:142422

REFERENCE 3: 144:135244

REFERENCE 4: 144:135239

REFERENCE 5: 144:126725

REFERENCE 6: 144:114444

REFERENCE 7: 144:105009

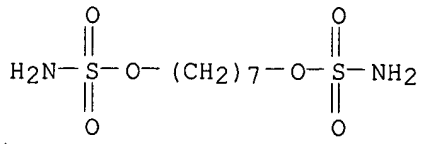
REFERENCE 8: 144:80862

REFERENCE 9: 144:64351

REFERENCE 10: 144:50043

L58 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN **96892-57-8** REGISTRY
ED Entered STN: 23 Jun 1985
CN Sulfamic acid, 1,7-heptanediyl ester (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1,7-Heptanediol disulfamate
CN 1,7-Heptanediyl sulfamate
CN Hepsulfam
CN NCI 329680
CN NSC 329680

FS 3D CONCORD
MF C7 H18 N2 O6 S2
LC STN Files: ADISINSIGHT, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSRESEARCH, IPA, MEDLINE, PHAR, PROUSDDR, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

32 REFERENCES IN FILE CA (1907 TO DATE)
33 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 142:211434

REFERENCE 2: 141:420029

REFERENCE 3: 141:167110

REFERENCE 4: 141:64376

REFERENCE 5: 140:175172

REFERENCE 6: 137:237714

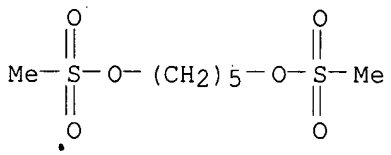
REFERENCE 7: 137:88442

REFERENCE 8: 134:50996

REFERENCE 9: 133:217357

REFERENCE 10: 133:144613

L58 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN **2374-22-3** REGISTRY
ED Entered STN: 16 Nov 1984
CN 1,5-Pentanediol, dimethanesulfonate (7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Methanesulfonic acid, pentamethylene ester (6CI)
OTHER NAMES:
CN 1,5-Dimesyloxypentane
CN NSC 17019
CN Pentasulfan
CN Pentasulphan
FS 3D CONCORD
MF C7 H16 O6 S2
CI COM
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CHEMLIST, IFICDB, IFIPAT, IFIUDB, RTECS*, SPECINFO, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

34 REFERENCES IN FILE CA (1907 TO DATE)
34 REFERENCES IN FILE CAPLUS (1907 TO DATE)
7 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 140:175172

REFERENCE 2: 134:50996

REFERENCE 3: 132:222523

REFERENCE 4: 132:133710

REFERENCE 5: 129:95608

REFERENCE 6: 126:89349

REFERENCE 7: 115:84832

REFERENCE 8: 108:21357

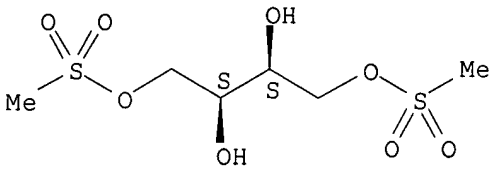
REFERENCE 9: 105:72213

REFERENCE 10: 100:200855

L58 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN **299-75-2** REGISTRY
ED Entered STN: 16 Nov 1984
CN 1,2,3,4-Butanetetrol, 1,4-dimethanesulfonate, (2S,3S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,2,3,4-Butanetetrol, 1,4-dimethanesulfonate, [S-(R*,R*)]-
CN Threitol, 1,4-dimethanesulfonate, (2S,3S)- (8CI)
OTHER NAMES:
CN (2S,3S)-Threitol 1,4-bismethanesulfonate
CN L-Threitol 1,4-bis(methanesulfonate)
CN NSC 39069
CN Ovastat
CN Threosulphan
CN Treosulfan
CN Treosulphan
CN Tresulfan
FS STEREOSEARCH
DR 14461-01-9, 5592-88-1, 27863-55-4
MF C6 H14 O8 S2
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CHEMINFORMRX, CHEMLIST, CIN, CSNB, DDFU, DRUGU, EMBASE, HSDB*, IMSDRUGNEWS, IMSRESEARCH, IPA, MEDLINE, MSDS-OHS, NIOSHTIC, PHAR, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

149 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
149 REFERENCES IN FILE CAPLUS (1907 TO DATE)
4 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 144:142166

REFERENCE 2: 144:64341

REFERENCE 3: 144:45462

REFERENCE 4: 143:477963

REFERENCE 5: 143:452847

REFERENCE 6: 143:405768

REFERENCE 7: 143:339208

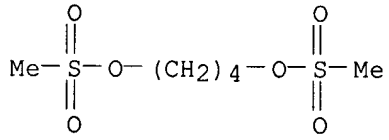
REFERENCE 8: 143:292623

REFERENCE 9: 143:278548

REFERENCE 10: 143:278537

L58 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN **55-98-1** REGISTRY
ED Entered STN: 16 Nov 1984
CN 1,4-Butanediol, dimethanesulfonate (8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Methanesulfonic acid, tetramethylene ester (6CI)
OTHER NAMES:
CN 1,4-Bis(methanesulfonoxy)butane
CN 1,4-Bis(methanesulfonyloxy)butane
CN 1,4-Butanediol dimesylate
CN 1,4-Dibutanediol dimethanesulfonate
CN 1,4-Dimethanesulfonoxybutane
CN 1,4-Dimethylsulfonyloxybutane
CN 2041CB
CN AN 33501
CN Busulfan
CN Busulfex

CN Busulphan
CN Butane-1,4-diyl bis(methanesulfonate)
CN CB 2041
CN Citosulfan
CN Glyzophrol
CN GT 2041
CN GT 41
CN Leucosulfan
CN Mablin
CN Mielevcin
CN Mielosan
CN Mielucin
CN Milecitan
CN Mileran
CN Misulban
CN Mitostan
CN Myeloleukon
CN Myelosan
CN Mylecytan
CN Myleran
CN NCI C01592
CN NSC 750
CN Sulfabutin
CN Sulphabutin
CN Tetramethylene bis[methanesulfonate]
CN X 149
FS 3D CONCORD
MF C6 H14 O6 S2
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SPECINFO, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1903 REFERENCES IN FILE CA (1907 TO DATE)
38 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1908 REFERENCES IN FILE CAPLUS (1907 TO DATE)
128 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 144:150398

REFERENCE 2: 144:141872

REFERENCE 3: 144:135225

REFERENCE 4: 144:121774

REFERENCE 5: 144:108368

REFERENCE 6: 144:100521

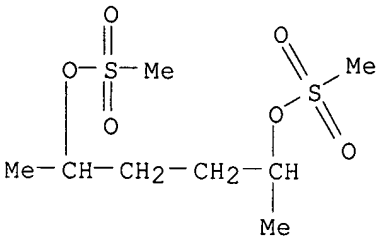
REFERENCE 7: 144:94400

REFERENCE 8: 144:94357

REFERENCE 9: 144:85770

REFERENCE 10: 144:81161

L58 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2006 ACS on STN
RN **55-93-6** REGISTRY
ED Entered STN: 16 Nov 1984
CN 2,5-Hexanediol, dimethanesulfonate (7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Methanesulfonic acid, 1,4-dimethyltetramethylene ester (6CI)
OTHER NAMES:
CN 1,4-Bis(methylsulfonyloxy)-1,4-dimethylbutane
CN Dimethylbusulfan
CN Dimethylmyleran
CN NSC 180541
CN NSC 180542
CN NSC 180543
CN NSC 23890
FS 3D CONCORD
DR 51900-84-6
MF C8 H18 O6 S2
LC STN Files: AGRICOLA, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CHEMINFORMRX, DDFU, DRUGU, EMBASE, MEDLINE, NIOSHTIC, RTECS*, SPECINFO, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

77 REFERENCES IN FILE CA (1907 TO DATE)
77 REFERENCES IN FILE CAPLUS (1907 TO DATE)
27 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 141:254551

REFERENCE 2: 140:175172

REFERENCE 3: 138:265631

REFERENCE 4: 137:290985

REFERENCE 5: 136:363828

REFERENCE 6: 134:131277

REFERENCE 7: 134:50996

REFERENCE 8: 131:4246

REFERENCE 9: 122:45833

REFERENCE 10: 115:270237

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 15:16:32 ON 28 FEB 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 28 Feb 2006 VOL 144 ISS 10
FILE LAST UPDATED: 27 Feb 2006 (20060227/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> => d l57 bib abs hitind hitstr retable tot

L57 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:162592 HCAPLUS
DN 140:175172
TI Use of **treosulfan** and derivatives thereof for treating **multiple sclerosis**
IN **Sass, Gretel**
PA Medac Gesellschaft Fur Klinische Spezialpraparate MBH, Germany
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2004016263 A1 20040226 WO 2003-EP8957 20030812 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
DE 10237146 A1 20040304 DE 2002-10237146 20020813 <--
AU 2003255429 A1 20040303 AU 2003-255429 20030812 <--
EP 1528922 A1 20050511 EP 2003-787778 20030812 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
JP 2006500357 T2 20060105 JP 2004-528477 20030812 <--
US 2006041015 A1 20060223 US 2005-524144 20050726 <--
PRAI DE 2002-10237146 A 20020813 <--
WO 2003-EP8957 W 20030812 <--

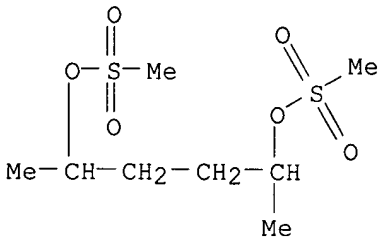
AB The invention discloses the use of **treosulfan** and/or derivs. thereof for producing a pharmaceutical composition used in the treatment of **multiple sclerosis**.

IC ICM A61K0031-21
CC 1-11 (Pharmacology)
Section cross-reference(s): 63
ST **treosulfan multiple sclerosis** treatment; **multiple sclerosis** treatment **treosulfan** deriv
IT Drug delivery systems
(infusions; **treosulfan** and derivs. for treatment of **multiple sclerosis**)
IT Drug delivery systems
(oral; **treosulfan** and derivs. for treatment of **multiple sclerosis**)
IT **Multiple sclerosis**
Nervous system agents
(**treosulfan** and derivs. for treatment of **multiple sclerosis**)
IT Interleukin 12
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**treosulfan** and derivs. for treatment of **multiple sclerosis**)
IT Immunomodulators
(**treosulfan** and derivs. for treatment of **multiple sclerosis**, and use with other agents)
IT **Interferons**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**treosulfan** and derivs. for treatment of **multiple sclerosis**, and use with other agents)
IT **55-93-6, Dimethylbusulfan 55-98-1, Busulfan 299-75-2, Treosulfan 299-75-2D, Treosulfan**, derivs. **2374-22-3, Pentasulfan 96892-57-8, Hepsulfam**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**treosulfan** and derivs. for treatment of **multiple sclerosis**)
IT **147245-92-9, Glatiramer acetate**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

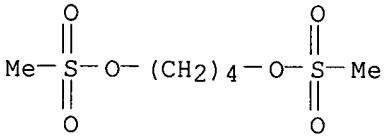
(Biological study); USES (Uses)
(**treosulfan** and derivs. for treatment of **multiple sclerosis**, and use with other agents)

IT **55-93-6, Dimethylbusulfan 55-98-1, Busulfan 299-75-2, Treosulfan 299-75-2D** * , ***Treosulfan**, derivs. **2374-22-3, Pentasulfan 96892-57-8, Hepsulfam**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**treosulfan** and derivs. for treatment of **multiple sclerosis**)

RN 55-93-6 HCAPLUS
CN 2,5-Hexanediol, dimethanesulfonate (7CI, 8CI, 9CI) (CA INDEX NAME)

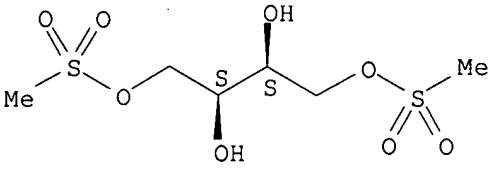


RN 55-98-1 HCAPLUS
CN 1,4-Butanediol, dimethanesulfonate (8CI, 9CI) (CA INDEX NAME)



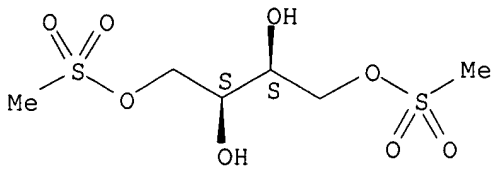
RN 299-75-2 HCAPLUS
CN 1,2,3,4-Butanetetrol, 1,4-dimethanesulfonate, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

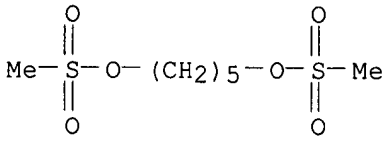


RN 299-75-2 HCAPLUS
CN 1,2,3,4-Butanetetrol, 1,4-dimethanesulfonate, (2S,3S)- (9CI) (CA INDEX NAME)

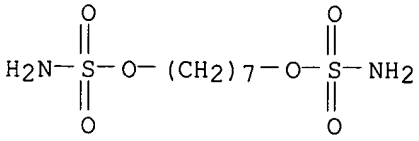
Absolute stereochemistry.



RN 2374-22-3 HCAPLUS
CN 1,5-Pentanediol, dimethanesulfonate (7CI, 8CI, 9CI) (CA INDEX NAME)



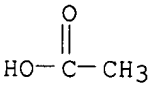
RN 96892-57-8 HCAPLUS
CN Sulfamic acid, 1,7-heptanediyl ester (9CI) (CA INDEX NAME)



IT **147245-92-9, Glatiramer acetate**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**treosulfan** and derivs. for treatment of **multiple sclerosis**, and use with other agents)
RN 147245-92-9 HCAPLUS
CN L-Glutamic acid, polymer with L-alanine, L-lysine and L-tyrosine, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 64-19-7
CMF C2 H4 O2



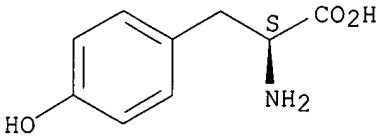
CM 2

CRN 28704-27-0
CMF (C9 H11 N O3 . C6 H14 N2 O2 . C5 H9 N O4 . C3 H7 N O2)x
CCI PMS

CM 3

CRN 60-18-4
CMF C9 H11 N O3

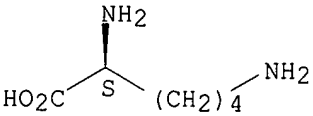
Absolute stereochemistry. Rotation (-).



CM 4

CRN 56-87-1
CMF C6 H14 N2 O2

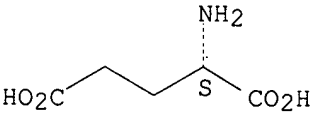
Absolute stereochemistry.



CM 5

CRN 56-86-0
CMF C5 H9 N O4

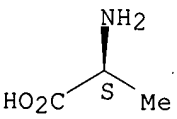
Absolute stereochemistry.



CM 6

CRN 56-41-7
CMF C3 H7 N O2

Absolute stereochemistry. Rotation (+).



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Baumgart, J	2001			WO 0132154 A	HCAPLUS
Openshaw, H	2000	6	563	BIOLOGY OF BLOOD AND	HCAPLUS

L57 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:754995 HCAPLUS
DN 137:268473
TI Porous drug matrices and methods of manufacture thereof
IN Straub, Julie; Altreuter, David; Bernstein, Howard; Chickering, Donald E.; Khattak, Sarwat; Randall, Greg
PA Acusphere Inc., USA
SO U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U. S. 6,395,300.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002142050	A1	20021003	US 2002-53929	20020122
	US 6395300	B1	20020528	US 1999-433486	19991104
	US 6645528	B1	20031111	US 2000-694407	20001023
	US 6932983	B1	20050823	US 2000-706045	20001103
	ZA 2001010347	A	20030730	ZA 2001-10347	20011218
	US 2005048116	A1	20050303	US 2004-924642	20040824
	US 2005058710	A1	20050317	US 2004-928886	20040827
PRAI	US 1999-136323P	P	19990527		
	US 1999-158659P	P	19991008		
	US 1999-433486	A2	19991104		
	US 2002-53929	A3	20020122		

AB Drugs, especially low aqueous solubility drugs, are provided in a porous matrix form, preferably microparticles, which enhances dissoln. of the drug in aqueous media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aqueous solubility, in a volatile solvent to form a drug solution, (ii) combining at least one pore forming agent with the drug solution to form an emulsion, suspension, or second solution and hydrophilic or hydrophobic excipients that stabilize the drug and inhibit crystallization, and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second solution to yield the porous matrix of drug. Hydrophobic or hydrophilic excipients may be selected to stabilize the drug in crystalline form by inhibiting crystal growth or to stabilize the drug in amorphous form by preventing crystallization The pore forming agent can be either a volatile liquid that is immiscible with the drug solvent or a volatile solid compound, preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aqueous medium and administered parenterally, or processed using standard techniques into tablets or capsules for oral administration. Thus, 5.46 g of PEG 8000, 0.545 g of prednisone, and 0.055 g of Span 40 were dissolved in 182 mL of methylene chloride. A solution of 3.27 g of ammonium bicarbonate in 18.2 mL of water was added to the organic solution (phase ratio 1:10) and homogenized for 5 min at 16,000 RPM. The resulting emulsion was spray dried on a benchtop spray dryer using an air-atomizing nozzle and nitrogen as the drying gas.

IC ICM A61K0009-14
ICS A61K0009-50
INCL 424499000
CC 63-6 (Pharmaceuticals)

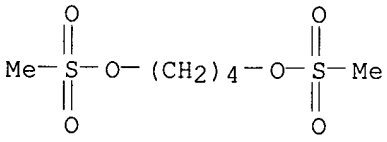
IT Amino acids, biological studies
Carbohydrates, biological studies
Granulocyte colony-stimulating factor receptors
Interferons
Interleukins
Lecithins
Polymers, biological studies
Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(porous drug matrixes and methods of manufacture thereof)

IT 50-28-2, Estradiol, biological studies 50-35-1, Thalidomide 52-53-9, Verapamil 53-03-2, Prednisone **55-98-1**, **Busulfan** 57-63-6, Ethinyl estradiol 58-61-7, Adenosine, biological studies 59-92-7, Levodopa, biological studies 67-78-7 67-97-0, Vitamin D3 71-58-9, Medroxyprogesterone acetate 75-64-9, Erbumine, biological studies 77-36-1, Chlorthalidone 89-57-6, Mesalamine 126-07-8, Griseofulvin 128-13-2, Ursodiol 298-46-4, Carbamazepine 302-79-4, Tretinoin 321-64-2, Tacrine 363-24-6, Dinoprostone 437-38-7, Fentanyl 439-14-5, Diazepam 443-48-1, Metronidazole 518-28-5, Podofilox 631-61-8, Ammonium acetate 657-24-9, Metformin 745-65-3, Alprostadil 846-49-1, Lorazepam 1066-33-7, Ammonium bicarbonate 1863-63-4, Ammonium benzoate 1951-25-3, Amiodarone 3239-44-9, Dexfenfluramine 4759-48-2, Isotretinoin 5534-09-8, Beclomethasone dipropionate 5593-20-4, Betamethasone dipropionate 9002-68-0, Follitropin 9002-72-6, Growth hormone 9005-65-6, Tween 80 9007-12-9, Calcitonin 9041-93-4, Bleomycin sulfate 10238-21-8, Glyburide 11096-26-7, Erythropoietin 12125-02-9, Ammonium chloride, biological studies 12629-01-5, Somatropin 12633-72-6, Amphotericin 13311-84-7, Flutamide 15307-79-6, Diclofenac sodium 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 18559-94-9, Albuterol 20830-75-5, Digoxin 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 22204-53-1, Naproxen 25322-68-3, Polyethylene glycol 26266-57-9, Span 40 27203-92-5, Tramadol 28860-95-9, Carbidopa 28981-97-7, Alprazolam. 29094-61-9, Glipizide 30516-87-1, Zidovudine 32986-56-4, Tobramycin 33069-62-4, Paclitaxel 34911-55-2, Bupropion 36505-84-7, Buspirone 40391-99-9 41340-25-4, Etodolac 41575-94-4, Carboplatin 42399-41-7, Diltiazem 42924-53-8, Nabumetone 51333-22-3, Budesonide 51773-92-3, Mefloquine hydrochloride 54143-55-4, Flecainide 54527-84-3, Nicardipine hydrochloride 54910-89-3, Fluoxetine 54965-21-8, Albendazole 54965-24-1, Tamoxifen citrate 55268-75-2, Cefuroxime 56124-62-0, Valrubicin 56180-94-0, Acarbose 60142-96-3, Gabapentin 60205-81-4, Ipratropium. 63659-18-7, Betaxolol 65277-42-1, Ketoconazole 66085-59-4, Nimodipine 66376-36-1, Alendronate 66852-54-8, Halobetasol propionate 68693-11-8, Modafinil 69655-05-6, Didanosine 70476-82-3, Mitoxantrone hydrochloride 72432-03-2, Miglitol 72509-76-3, Felodipine 72558-82-8, Ceftazidime 72956-09-3, Carvedilol 73384-59-5, Ceftriaxone 73590-58-6, Omeprazole 75330-75-5, Lovastatin 75695-93-1, Isradipine 75847-73-3, Enalapril 76095-16-4, Enalapril maleate 76547-98-3, Lisinopril 76824-35-6, Famotidine 76963-41-2, Nizatidine 77883-43-3, Doxazosin mesylate 78246-49-8, Paroxetine hydrochloride 78628-80-5, Terbinafine hydrochloride 78755-81-4, Flumazenil 79517-01-4, Octreotide acetate 79559-97-0, Sertraline hydrochloride 79794-75-5, Loratadine 79902-63-9, Simvastatin 80274-67-5, Metoprolol fumarate 81098-60-4, Cisapride 81103-11-9, Clarithromycin 82410-32-0, Ganciclovir 82752-99-6, Nefazodone hydrochloride 82834-16-0, Perindopril 83799-24-0, Fexofenadine 83905-01-5, Azithromycin 83919-23-7, Mometasone furoate 84625-61-6, Itraconazole 86386-73-4, Fluconazole 86541-74-4, Benazepril hydrochloride 86541-75-5, Benazepril 87679-37-6, Trandolapril 89778-27-8, Toremifene citrate 90566-53-3, Fluticasone 91161-71-6, Terbinafine 91421-42-0, Rubitecan

93413-69-5, Venlafaxine 93957-54-1, Fluvastatin 95058-81-4, Gemcitabine 95233-18-4, Atovaquone 97048-13-0, Urofollitropin 97322-87-7, Troglitazone 98048-97-6, Fosinopril 98079-52-8, Lomefloxacin hydrochloride 98319-26-7, Finasteride 99011-02-6, Imiquimod 99294-93-6, Zolpidem tartrate 100286-90-6, Irinotecan hydrochloride 100986-85-4, Levofloxacin 103577-45-3, Lansoprazole 103628-48-4, Sumatriptan succinate 103775-10-6, Moexipril 104227-87-4, Famciclovir 104632-25-9, Pramipexole dihydrochloride 106266-06-2, Risperidone 106392-12-5, Pluronic f127 106463-17-6, Tamsulosin hydrochloride 106685-40-9, Adapalene 107753-78-6, Zafirlukast 109889-09-0, Granisetron 110871-86-8, Sparfloxacin 111470-99-6, Amlodipine besylate 111974-72-2, Quetiapine fumarate 112809-51-5, Letrozole 113806-05-6, Olopatadine 114798-26-4, Losartan 114977-28-5, Docetaxel 115956-12-2, Dolasetron 120014-06-4, Donepezil 124832-26-4, Valacyclovir 127779-20-8, Saquinavir 131918-61-1, Paricalcitol 132539-06-1, Olanzapine 134308-13-7, Tolcapone 134678-17-4, Lamivudine 137862-53-4, Valsartan 140678-14-4, Mangafodipir trisodium 142373-60-2, Tirofiban hydrochloride 144701-48-4, Telmisartan 145040-37-5, Candesartan cilexetil 147059-72-1, Trovafloxacin **147245-92-9, Glatiramer acetate** 150378-17-9, Indinavir 154248-97-2, Imiglucerase 154598-52-4, Efavirenz 155141-29-0, Rosiglitazone maleate 155213-67-5, Ritonavir 158966-92-8, Montelukast 159989-65-8, Nelfinavir mesylate 161814-49-9, Amprenavir 162011-90-7, Rofecoxib 169590-42-5, Celecoxib 171599-83-0, Sildenafil citrate 260779-88-2, Cisapride monohydrate 679809-58-6, Enoxaparin sodium
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(porous drug matrixes and methods of manufacture thereof)

IT **55-98-1, Busulfan 147245-92-9, Glatiramer acetate**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(porous drug matrixes and methods of manufacture thereof)

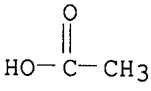
RN 55-98-1 HCAPLUS
CN 1,4-Butanediol, dimethanesulfonate (8CI, 9CI) (CA INDEX NAME)



RN 147245-92-9 HCAPLUS
CN L-Glutamic acid, polymer with L-alanine, L-lysine and L-tyrosine, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 64-19-7
CMF C2 H4 O2



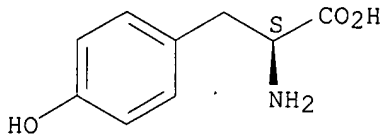
CM 2

CRN 28704-27-0
CMF (C9 H11 N O3 . C6 H14 N2 O2 . C5 H9 N O4 . C3 H7 N O2)x
CCI PMS

CM 3

CRN 60-18-4
CMF C9 H11 N O3

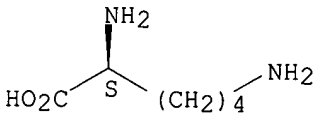
Absolute stereochemistry. Rotation (-).



CM 4

CRN 56-87-1
CMF C6 H14 N2 O2

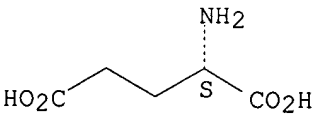
Absolute stereochemistry.



CM 5

CRN 56-86-0
CMF C5 H9 N O4

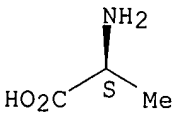
Absolute stereochemistry.



CM 6

CRN 56-41-7
CMF C3 H7 N O2

Absolute stereochemistry. Rotation (+).



L57 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:861473 HCAPLUS
DN 134:32972
TI Porous drug matrixes containing polymers and sugars and methods of their manufacture
IN Straub, Julie; Bernstein, Howard; Chickering, Donald E., III; Khatak, Sarwat; Randall, Greg
PA Acusphere, Inc., USA
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000072827	A2	20001207	WO 2000-US14578	20000525
	WO 2000072827	A3	20010125		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6395300	B1	20020528	US 1999-433486	19991104
	CA 2371836	AA	20001207	CA 2000-2371836	20000525
	CA 2371836	C	20060131		
	EP 1180020	A2	20020220	EP 2000-939365	20000525
	EP 1180020	B1	20051214		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY				
	BR 2000010984	A	20020430	BR 2000-10984	20000525
	JP 2003500438	T2	20030107	JP 2000-620939	20000525
	NZ 516083	A	20030829	NZ 2000-516083	20000525
	AU 768022	B2	20031127	AU 2000-54459	20000525
	AT 312601	E	20051215	AT 2000-939365	20000525
	US 2002041896	A1	20020411	US 2001-798824	20010302
	US 6610317	B2	20030826		
	NO 2001005753	A	20020128	NO 2001-5753	20011126
	ZA 2001010347	A	20030730	ZA 2001-10347	20011218
PRAI	US 1999-136323P	P	19990527		
	US 1999-158659P	P	19991008		
	US 1999-433486	A	19991104		
	US 2000-186310P	P	20000302		
	WO 2000-US14578	W	20000525		

AB Drugs, especially low aqueous solubility drugs, are provided in a porous matrix form, preferably microparticles, which enhances dissoln. of the drug in aqueous media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aqueous solubility, in a volatile solvent to form a drug solution, (ii) combining at least one pore forming agent with the drug solution to form an emulsion, suspension, or second solns., and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second solution to yield the porous matrix of drug. The pore forming agent can be either a volatile liquid that is immiscible with the drug solvent or a volatile solid compound, preferably

a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aqueous medium and administered parenterally, or processed using standard techniques into tablets or capsules for oral administration. Paclitaxel or docetaxel can be provided in a porous matrix form, which allows the drug to be formulated without solubilizing agents and administered as a bolus. For example, a nifedipine-loaded organic solution was prepared by dissolving 9.09 g of PEG 3350, 2.27 g of nifedipine, and 0.009 g of lecithin in 182 mL of methylene chloride. An aqueous solution was prepared by dissolving 3.27 g of NH4HCO3 and 0.91 g of PEG 3350 in 1.82 mL of water. The aqueous and organic solns. were homogenized and resulting emulsion was spray dried. A suspension of the porous nifedipine drug matrix was prepared in 5% dextrose solution at a concentration of 2.5 mg/mL. A bolus injection of the suspension was tolerated when administrated to dogs.

IC ICM A61K0009-16

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

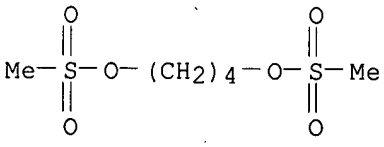
IT **Interferons**
Interleukins
Taxanes
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT 50-28-2, Estradiol, biological studies 50-35-1, Thalidomide 50-99-7, Dextrose, biological studies 52-53-9, Verapamil 53-03-2, Prednisone **55-98-1**, **Busulfan** 57-63-6, Ethinyl estradiol 58-61-7, Adenosine, biological studies 59-92-7, Levodopa, biological studies 67-78-7 67-97-0, Vitamin D3 67-97-0D, Vitamin D3, analogs 71-58-9, Medroxyprogesterone acetate 75-64-9, Erbumine, biological studies 77-36-1, Chlorthalidone 89-57-6, Mesalamine 126-07-8, Griseofulvin 128-13-2, Ursodiol 298-46-4, Carbamazepine 302-79-4, Tretinoin 321-64-2, Tacrine 363-24-6, Dinoprostone 437-38-7, Fentanyl 439-14-5, Diazepam 443-48-1, Metronidazole 518-28-5, Podofilox 745-65-3, Alprostadil 846-49-1, Lorazepam 1951-25-3, Amiodarone 3239-44-9, Dexfenfluramine 4759-48-2, Isotretinoin 5534-09-8, Beclomethasone dipropionate 5593-20-4, Betamethasone dipropionate 9002-68-0, Follitropin 9002-72-6, Growth hormone 9007-12-9, Calcitonin 9041-93-4, Bleomycin sulfate 10238-21-8, Glyburide 11096-26-7, Erythropoietin 12629-01-5, Somatropin 12633-72-6, Amphotericin 13311-84-7, Flutamide 15307-79-6, Diclofenac sodium 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 18559-94-9, Albuterol 20830-75-5, Digoxin 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 22204-53-1, Naproxen 27203-92-5, Tramadol 28860-95-9, Carbidopa 28981-97-7, Alprazolam 29094-61-9, Glipizide 30516-87-1, Zidovudine 32986-56-4, Tobramycin 33069-62-4, Paclitaxel 34911-55-2, Bupropion 36505-84-7, Buspirone 40391-99-9 41340-25-4, Etodolac 41575-94-4, Carboplatin 42399-41-7, Diltiazem 42924-53-8, Nabumetone 51022-70-9, Albuterol sulfate 51333-22-3, Budesonide 51773-92-3, Mefloquine hydrochloride 54143-55-4, Flecainide 54527-84-3, Nicardipine hydrochloride 54910-89-3, Fluoxetine 54965-21-8, Albendazole 54965-24-1, Tamoxifen citrate 55268-75-2, Cefuroxime 56124-62-0, Valrubicin 56180-94-0, Acarbose 59729-33-8, Citalopram

60142-96-3, Gabapentin 60205-81-4, Ipratropium 63659-18-7, Betaxolol
65277-42-1, Ketoconazole 66085-59-4, Nimodipine 66376-36-1,
Alendronate 66852-54-8, Halobetasol propionate 69655-05-6, Didanosine
70476-82-3, Mitoxantrone hydrochloride 72432-03-2, Miglitol
72509-76-3, Felodipine 72558-82-8, Ceftazidime 72956-09-3, Carvedilol
73384-59-5, Ceftriaxone 73590-58-6, Omeprazole 75330-75-5, Lovastatin
75695-93-1, Isradipine 75847-73-3, Enalapril 76095-16-4, Enalapril
maleate 76547-98-3, Lisinopril 76824-35-6, Famotidine 76963-41-2,
Nizatidine 77883-43-3, Doxazosin mesylate 78246-49-8, Paroxetine
hydrochloride 78628-80-5, Terbinafine hydrochloride 78755-81-4,
Flumazenil 79517-01-4, Octreotide acetate 79559-97-0, Sertraline
hydrochloride 79794-75-5, Loratadine 79902-63-9, Simvastatin
80274-67-5, Metoprolol fumarate 81098-60-4, Cisapride 81103-11-9,
Clarithromycin 82410-32-0, Ganciclovir 82752-99-6, Nefazodone
hydrochloride 82834-16-0, Perindopril 83799-24-0, Fexofenadine
83905-01-5, Azithromycin 83919-23-7, Mometasone furoate 84625-61-6,
Itraconazole 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole
86541-74-4, Benazepril hydrochloride 86541-75-5, Benazepril
87679-37-6, Trandolapril 89778-27-8, Toremifene citrate 91161-71-6,
Terbinafine 91421-42-0, Rubitecan 93413-69-5, Venlafaxine
93957-54-1, Fluvastatin 95058-81-4, Gemcitabine 95233-18-4, Atovaquone
97048-13-0, Urofollitropin 97322-87-7, Troglitazone 98048-97-6,
Fosinopril 98079-52-8, Lomefloxacin hydrochloride 98319-26-7,
Finasteride 99011-02-6, Imiquimod 99294-93-6, Zolpidem tartrate
100286-90-6, Irinotecan hydrochloride 100986-85-4, Levofloxacin
103577-45-3, Lansoprazole 103628-48-4, Sumatriptan succinate
103775-10-6, Moexipril 104227-87-4, Famciclovir 104632-25-9,
Pramipexole dihydrochloride 106266-06-2, Risperidone 106463-17-6,
Tamsulosin hydrochloride 106685-40-9, Adapalene 107753-78-6,
Zafirlukast 109889-09-0, Granisetron 110871-86-8, Sparfloxacin
111470-99-6, Amlodipine besylate 111974-72-2, Quetiapine fumarate
112809-51-5, Letrozole 113806-05-6, Olopatadine 114798-26-4, Losartan
114977-28-5, Docetaxel 115956-12-2, Dolasetron 120014-06-4, Donepezil
124832-26-4, Valacyclovir 127779-20-8, Saquinavir 131918-61-1,
Paricalcitol 132539-06-1, Olanzapine 134308-13-7, Tolcapone
134678-17-4, Lamivudine 137862-53-4, Valsartan 140678-14-4,
Mangafodipir trisodium 142373-60-2, Tirofiban hydrochloride
143011-72-7, Granulocyte colony-stimulating factor 144701-48-4,
Telmisartan 145040-37-5, Candesartan cilexetil 147059-72-1,
Trovafloxacin **147245-92-9, Glatiramer acetate**
150378-17-9, Indinavir 154248-97-2, Imiglucerase 154598-52-4,
Efavirenz 155141-29-0, Rosiglitazone maleate 155213-67-5, Ritonavir
158966-92-8, Montelukast 159989-65-8, Nelfinavir mesylate 161814-49-9,
Amprenavir 162011-90-7, Rofecoxib 169590-42-5, Celecoxib
171599-83-0, Sildenafil citrate 679809-58-6, Enoxaparin sodium
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of porous matrixes containing hydrophilic polymers and sugars
for
enhancement of drug dissoln.)

IT **55-98-1, Busulfan 147245-92-9,**
Glatiramer acetate
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of porous matrixes containing hydrophilic polymers and sugars
for
enhancement of drug dissoln.)

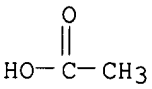
RN 55-98-1 HCAPLUS
CN 1,4-Butanediol, dimethanesulfonate (8CI, 9CI) (CA INDEX NAME)



RN 147245-92-9 HCAPLUS
CN L-Glutamic acid, polymer with L-alanine, L-lysine and L-tyrosine, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 64-19-7
CMF C2 H4 O2



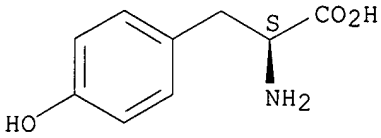
CM 2

CRN 28704-27-0
CMF (C9 H11 N O3 . C6 H14 N2 O2 . C5 H9 N O4 . C3 H7 N O2)x
CCI PMS

CM 3

CRN 60-18-4
CMF C9 H11 N O3

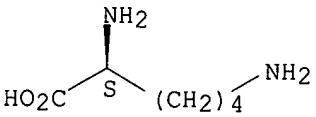
Absolute stereochemistry. Rotation (-).



CM 4

CRN 56-87-1
CMF C6 H14 N2 O2

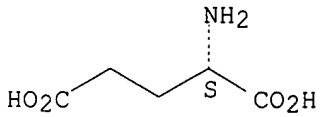
Absolute stereochemistry.



CM 5

CRN 56-86-0
CMF C5 H9 N O4

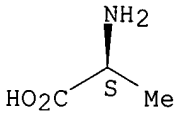
Absolute stereochemistry.



CM 6

CRN 56-41-7
CMF C3 H7 N O2

Absolute stereochemistry. Rotation (+).



L57 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
AN **2000:838541** HCAPLUS
DN 135:45042
TI Peripheral blood stem cell transplantation in **multiple sclerosis** with **busulfan** and cyclophosphamide conditioning: Report of toxicity and immunological monitoring
AU Openshaw, Harry; Lund, Brett T.; Kashyap, Ashwin; Atkinson, Roscoe; Sniecinski, Irena; Weiner, Leslie P.; Forman, Stephen
CS Department of Neurology, City of Hope National Medical Center, Duarte, CA, USA
SO Biology of Blood and Marrow Transplantation (2000), 6(5a), 563-575
CODEN: BBMTF6; ISSN: 1083-8791
PB Carden Jennings Publishing
DT Journal
LA English
AB **Multiple sclerosis** (MS) is an immune-mediated disease that may be amenable to high-dose immunosuppression with peripheral blood stem cell transplantation (SCT) in selected patients. Five MS patients (all women, ages 39-47 yr) received granulocyte colony-stimulating factor (G-CSF) for stem cell mobilization, CD34 cell selection for T-cell depletion, a preparatory regimen of **busulfan** (1 mg/kg + 16 doses) and cyclophosphamide (120 mg/kg), and antithymocyte globulin (10 mg/kg + 3 doses) at the time of stem cell infusion. Days required to recover absolute neutrophil count >500 were 12 to 14 and platelet count >20,000 were 17 to 58. Posttransplantation infectious complications in the first year after SCT occurred in 3 of 5 patients, and 1 patient died at day 22 after SCT from influenza A pneumonia. Neuropathol. study in this patient showed demyelinating plaques with surrounding macrophages but only rare T cells. In 2 patients, MS flared transiently with G-CSF. Magnetic resonance imaging gadolinium enhancement was present in 3 of 5 patients before transplantation and 0 of 4 after SCT. There were cerebrospinal fluid oligoclonal bands at 1 yr after SCT, similar to the pretransplantation assays. Sustained suppression of peripheral blood

mononuclear cell proliferative responses to myelin antigens occurred after SCT, but new responses to some myelin peptide fragments also developed after SCT. In 1 patient, enzyme-linked immunospot (ELISPOT) assays done 9 mo after SCT showed a predominant T helper 2 (Th2) cytokine pattern. Neurol. progression of 1 point on the extended disability status scale was seen in 1 patient 17 mo after SCT. Another patient who was neurol. stable died abruptly 19 mo after SCT from overwhelming S. pneumoniae sepsis. The remaining patients have had stable MS (follow-up, 18 and 30 mo). In summary, our experience confirms the high-risk nature of this approach. Further studies and longer follow-up would be needed to determine the significance of new lymphocyte proliferative responses after SCT and the overall effect of this treatment on the natural history of MS.

CC 15-8 (Immunochemistry)
Section cross-reference(s): 2

ST blood stem transplantation **multiple sclerosis**
busulfan cyclophosphamide CSF

IT Immunoglobulins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antithymocyte globulins; peripheral blood stem cell transplantation in **multiple sclerosis** with **busulfan**, cyclophosphamide and other drugs conditioning in report of toxicity and immunol. monitoring)

IT Nerve, disease
(demyelination; peripheral blood stem cell transplantation in **multiple sclerosis** with **busulfan**, cyclophosphamide and other drugs conditioning in report of toxicity and immunol. monitoring)

IT Immunosuppressants
Mononuclear cell (leukocyte)
(peripheral blood stem cell transplantation in **multiple sclerosis** with **busulfan**, cyclophosphamide and other drugs conditioning in report of toxicity and immunol. monitoring)

IT Hematopoietic precursor cell
(stem; peripheral blood stem cell transplantation in **multiple sclerosis** with **busulfan**, cyclophosphamide and other drugs conditioning in report of toxicity and immunol. monitoring)

IT **Multiple sclerosis**
(therapeutic agents; peripheral blood stem cell transplantation in **multiple sclerosis** with **busulfan**, cyclophosphamide and other drugs conditioning in report of toxicity and immunol. monitoring)

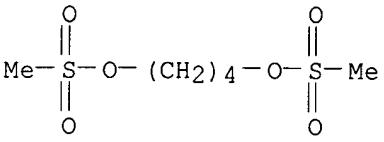
IT 50-18-0, Cyclophosphamide **55-98-1, Busulfan**
143011-72-7, Granulocyte-colony stimulating factor
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peripheral blood stem cell transplantation in **multiple sclerosis** with **busulfan**, cyclophosphamide and other drugs conditioning in report of toxicity and immunol. monitoring)

IT 58-73-1, Diphenhydramine 83-43-2, Methylprednisolone 103-90-2, Acetaminophen 100986-85-4, Levofloxacin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peripheral blood stem cell transplantation in **multiple sclerosis** with **busulfan**, cyclophosphamide and other drugs conditioning in report of toxicity and immunol. monitoring)

IT **55-98-1, Busulfan**
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(peripheral blood stem cell transplantation in **multiple sclerosis** with **busulfan**, cyclophosphamide and other drugs conditioning in report of toxicity and immunol. monitoring)

RN 55-98-1 HCAPLUS
CN 1,4-Butanediol, dimethanesulfonate (8CI, 9CI) (CA INDEX NAME)



RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Allegretta, M	1990	247	718	Science	MEDLINE
Azzaralli, B	1998	57	489	J Neuropath Exp Neur	
Baig, S	1991	33	73	Scand J Immunol	MEDLINE
Becker, C	1995	52	1985	Am J Health Syst Pha	HCAPLUS
Beutler, E	1996	93	1716	Proc Natl Acad Sci U	HCAPLUS
Bieganowska, K	1997	185	1585	J Exp Med	HCAPLUS
Birnbaum, G	1993	34	18	Ann Neurol	MEDLINE
Burt, R	1998	92	3505	Blood	HCAPLUS
Burt, R	1995	41	526	J Neurosci Res	HCAPLUS
Chiang, C	1991	566	265	Brain Res	HCAPLUS
Chou, Y	1992	38	105	J Neuroimmunol	HCAPLUS
Correale, J	1995	45	1370	Neurology	MEDLINE
de Rosbo, K	1993	92	2602	J Clin Invest	
Elson, L	1958	4	355	Br J Haematol	MEDLINE
Euler, H	1997	24	2153	J Rheumatol	HCAPLUS
Farhey, Y	1995	22	1179	J Rheumatol	MEDLINE
Fassas, A	1997	20	631	Bone Marrow Transpla	MEDLINE
Fujinami, R	1985	230	1043	Science	HCAPLUS
Goodkin, D	1995	37	30	Ann Neurol	MEDLINE
Hafler, D	1988	167	1313	J Exp Med	HCAPLUS
Hafler, D	1987	139	68	J Immunol	HCAPLUS
Hafler, D	1991	32	149	J Neuroimmunol	MEDLINE
Hartung, H	1999	52	A290	Neurology	
Hassan, M	1989	4	113	Bone Marrow Transpla	MEDLINE
Hauser, S	1986	19	578	Ann Neurol	MEDLINE
Hauser, S	1983	308	173	N Engl J Med	MEDLINE
Hobbs, J	1986	1	201	Bone Marrow Transpla	MEDLINE
Jain, K	1994	31	213	J Am Acad Dermatol	MEDLINE
Johnson, N	1987	2	203	Bone Marrow Transpla	MEDLINE
Kalman, B	1995	61	107	J Neuroimmunol	HCAPLUS
Kappos, L	1998	352	1491	Lancet	HCAPLUS
Kurtzke, J	1983	33	1444	Neurology	MEDLINE
Liblau, R	1991	21	1391	Eur J Immunol	HCAPLUS
Likosky, W	1991	54	1055	J Neurol Neurosurg P	MEDLINE
Lisak, R	1977	297	850	N Engl J Med	MEDLINE
Martin, R	1992	10	153	Annu Rev Immunol	HCAPLUS
McFarland, H	1995	37	419	Ann Neurol	MEDLINE
Mielcarek, M	1997	89	1629	Blood	HCAPLUS
Myers, L	1999	2	151	Frontiers in Multipl	
Olek, M	1996	39	684	Ann Neurol	MEDLINE
Olsson, T	1995	144	245	Immunol Rev	HCAPLUS

Openshaw, H	1997	3	202	Biol Blood Marrow Tr	MEDLINE
Openshaw, H	1991	7	411	Bone Marrow Transpla	MEDLINE
Openshaw, H	1996	78	1899	Cancer	HCAPLUS
Openshaw, H	2000	54	2147	Neurology	HCAPLUS
Panitch, H	1987	37	1097	Neurology	MEDLINE
Raine, C	1984	50	608	Lab Invest	MEDLINE
Rieckmann, P	1995	37	82	Ann Neurol	MEDLINE
Rudick, R	1997	42	379	Ann Neurol	MEDLINE
Santos, G	1993	20	12	Semin Oncol	HCAPLUS
Schumacher, G	1965	122	552	Ann N Y Acad Sci	
Slattery, J	1995	16	31	Bone Marrow Transpla	MEDLINE
Smith, R	1999	18	300	Curr Eye Res	MEDLINE
Somlo, G	1997	89	1521	Blood	HCAPLUS
Steinman, L	1996	85	299	Cell	HCAPLUS
Tourtellotte, W	1978	28	76	Neurology	HCAPLUS
Trapp, B	1998	338	278	N Engl J Med	MEDLINE
Trotter, J	1991	33	55	J Neuroimmunol	MEDLINE
van Gelder, M	1995	16	343	Bone Marrow Transpla	MEDLINE
Wallstrom, E	1998	28	3329	Eur J Immunol	MEDLINE
Weaver, C	1997	19	671	Bone Marrow Transpla	MEDLINE
Weinshenker, B	1991	114	1057	Brain	
Wekerle, H	1992	9	231	Int Rev Immunol	MEDLINE
Woodroofe, M	1993	5	583	Cytokine	HCAPLUS
Xu, S	1996	93	558	Br J Haematol	HCAPLUS

=> => fil wpix
FILE 'WPIX' ENTERED AT 15:30:44 ON 28 FEB 2006
COPYRIGHT (C) 2006 THE THOMSON CORPORATION

FILE LAST UPDATED: 27 FEB 2006 <20060227/UP>
MOST RECENT DERWENT UPDATE: 200614 <200614/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
GUIDES, PLEASE VISIT:
http://scientific.thomson.com/support/products/dwpi/

>>> FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT
DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX
FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS:
http://scientific.thomson.com/support/products/dwpifv/

>>> THE CPI AND EPI MANUAL CODES WILL BE REVISED FROM UPDATE 200601.
PLEASE CHECK:
http://scientific.thomson.com/support/patents/dwpiref/reftools/classification

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<
'BI ABEX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

=> d all abeq tech abex tot l90

L90 ANSWER 1 OF 2 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 2004-469056 [45] WPIX
DNC C2004-175837
TI Composition useful in the treatment of autoimmune diseases and neurological disorders e.g. **multiple sclerosis** and Alzheimer's disease comprises immunosuppressive agent and immunomodulatory compound.
DC B05
PA (MILD-I) MILDER D
CYC 1
PI AU 2003204344 A1 20031211 (200445)* 26 A61K031-52
ADT AU 2003204344 A1 AU 2003-204344 20030523
PRAI AU 2002-2492 20020523
IC ICM A61K031-52
ICS A61K038-03; A61K038-21; A61P015-00; **A61P025-28**; A61P037-04
AB AU2003204344 A UPAB: 20040716
NOVELTY - A composition comprises at least one immunosuppressive agent and at least one immunomodulatory compound.
ACTIVITY - Immunosuppressive; Neuroprotective; Nootropic; Antiinflammatory; Dermatological; Antiarthritic; Antirheumatic; Muscular-Gen.; Antiulcer; Gastrointestinal-Gen.; Hepatotropic; Immunostimulant; Antidiabetic; Antithyroid; Thyromimetic; Antiallergic; Vasotropic; CNS-Gen.; Antipsoriatic. A 50 year old woman with progressive **multiple sclerosis** was administered azathioprine (25 mg) orally and **interferon** beta -1b (8 millions units) by subcutaneous injection. The effect of the treatment was evaluated. The patient experienced sustained visual improvement, improved cerebellar functions and increased rationality and diminished disingibition when tested at 7 weeks.
MECHANISM OF ACTION - None given.
USE - In the treatment of autoimmune diseases and neurological disorders including **multiple sclerosis**, Alzheimer's disease, systemic lupus erythematosus, polyarthritis, ankylosing spondylitis, Crohn's disease, scleroderma, polymyositis, dermatomyositis, spondyloarthropathies (e.g. Sjogren's syndrome), ulcerative colitis, primary biliary cirrhosis and autoimmune hepatitis, Type 1 or immune-mediated diabetes mellitus, Grave's disease, Hashimoto's thyroiditis, autoimmune oophoritis and orchitis, autoimmune disease of the adrenal gland, temporal arteritis, anti-phospholipid syndrome, vasculitides (such as Wegener's granulomatosis), psoriasis, dermatitis herpetiformis, pemphigus vulgaris, vitiligo, Guillian-Barre disease and polychondritis; and for developing or promoting progressive **multiple sclerosis** or Alzheimer's disease medicine (claimed).
ADVANTAGE - The synergistic combination of immunosuppressive agent and immunomodulatory compound exhibits marked reversal of deficits associated with progressive **multiple sclerosis** such as progressive visual and neurological deficits and Alzheimer's disease. The composition reverses visual and cerebellar and cognitive deficits associated with **multiple sclerosis**.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B01-B01; B01-B02; B01-B03; B01-C02; B01-C03; B02-B; B02-C01; B02-D; B02-E; B02-I; B03-A; B04-B03A; B04-B03B; B04-C01A; B04-G01; B04-G21; B04-H05B; B04-L05C; B04-N04; B05-A03A; B05-B01J; B05-B01N; B06-H; B07-H; B08-D02; B10-A09B; B10-A10; B10-A13D; B10-B01A; B10-B02A; B10-B03B; B10-C02; B10-D03; B14-C06; B14-C09; B14-E08; B14-E10C;

B14-G02; B14-G03; B14-H01; B14-J01; B14-L06; B14-N11; B14-N12; B14-N17; **B14-S01**; B14-S04

TECH UPTX: 20040716

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The immunosuppressive agent is azathioprine, cyclophosphamide, cyclosporin, mycophenolate molefil and its salts, cytotoxic alkylating agent (preferably melphalan, carmustine, lomustine, cyclophosphamide, isophosphamide, chlorambucil, **busulfan**, temozolomide or thiotepa), antimetabolite (preferably paclitaxel, cytaribine, fluorouracil, gemcitabine hydrochloride, colaspase, hydroxyurea, cladribine, methotrexate sodium, mercaptopurine, docetaxel, raltitrexed or capecitabine), vinca alkaloids (preferably vindesine sulfate, vinorelbine tartrate or vinblastine sulfate), antibiotic cytotoxic (preferably doxorubicin hydrochloride, bleomycine sulfate, dactinomycin, daunorubicin hydrochloride, fludarabine phosphate, epirubicine hydrochloride, mitozantorane or idarubicin hydrochloride), hormonal antineoplastic agents (preferably nilutamide, cyporterone acetate, anasterozole, exemestane, bicalutamide, aminoglutethemide, cyproterone acetate, tamoxafin citrate, flutamide, toremifine, letrozole, fosfestrol sodium, leuprorelin acetate or groserelin acetate), or other neoplastic agents (preferably anagralide, amscarine, irinotecan hydrochloride, carboplatin, cisplatin, dacarbazine, etoposide, tratuzumab, altretamine, rituximab, tretinoim or teniposide). The immunomodulatory compound is **interferon** beta-1a/1b, **glatiramer acetate**, imiquimod, mycophenolate mofetil or its salts, **interferon** alpha-2b or a steroidal preparation (including hydrocortisone, dexamethasone, prednisone, prednisolone, methylprednisone or methylprednisolone acetate) (preferably **interferon** beta-1a, **interferon** beta-1b or **glatiramer acetate**).

ABEX UPTX: 20040716

ADMINISTRATION - The composition is administered at a dosage of 0.01 - 50 (preferably 0.1 - 10) mg/kg body weight. The **interferon** is administered at a dosage of 100000 - 50 millions (preferably 1 million - 10 millions) units/day or 0.5 - 200 mg/day or every second day. The administration is intravascularly, intraperitoneally, subcutaneously, intramuscularly or topically.

EXAMPLE - A composition comprising (mg): azathioprine (25 or 50) and **glatiramer acetate** (20) was prepared.

L90 ANSWER 2 OF 2 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 2004-226462 [21] WPIX
DNC C2004-089340
TI Treatment of **multiple sclerosis**, especially of secondary progressive type, by administration of **treosulfan** and/or its derivatives, e.g. **busulfan**.
DC B05
IN SASS, G
PA (MEDA-N) MEDAC GES KLINISCHE SPEZIALPRAEPARATE; (MEDA-N) MEDAC GES KLINISCHE SPZEIALPRAPARATE MBH
CYC 106
PI WO 2004016263 A1 20040226 (200421)* GE 37 A61K031-21
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
DE 10237146 A1 20040304 (200421) A61K031-255

AU 2003255429 A1 20040303 (200457) A61K031-21
EP 1528922 A1 20050511 (200532) GE A61K031-21
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
JP 2006500357 W 20060105 (200603) 16 A61K031-21
ADT WO 2004016263 A1 **WO 2003-EP8957 20030812**; DE 10237146 A1 **DE 2002-10237146 20020813**; AU 2003255429 A1 AU 2003-255429 20030812; EP 1528922 A1 EP 2003-787778 20030812, **WO 2003-EP8957 20030812**; JP 2006500357 W **WO 2003-EP8957 20030812**, JP 2004-528477 20030812
FDT AU 2003255429 A1 Based on WO 2004016263; EP 1528922 A1 Based on WO 2004016263; JP 2006500357 W Based on WO 2004016263
PRAI **DE 2002-10237146 20020813**
IC ICM A61K031-21; A61K031-255
ICS A61K038-21; A61K045-00; **A61P025-00**; A61P043-00
AB WO2004016263 A UPAB: 20040326
NOVELTY - The use of **treosulfan** (I) (i.e. L-threitol 1,4-bis-(methanesulfonate)) and/or its derivatives (I') is claimed in the treatment of **multiple sclerosis**.

ACTIVITY - Neuroprotective. In tests in rats with myelin-oligodendrocyte-glycoprotein induced experimental autoimmune encephaolmyelitis (an animal model of **multiple sclerosis**), 7/8 rats treated intraperitoneally with (I) at 1 g/kg on the day of immunization were still alive on day 53, compared with 2/8 in an untreated control group. No adverse hematological side-effects were caused by the treatment with (I).

MECHANISM OF ACTION - None given in the source material.

USE - For treatment of **multiple sclerosis**, specifically of the relapsing-remitting, primary progressive or secondary progressive type (all claimed), especially of the secondary progressive type. Treatment of five secondary progressive **multiple sclerosis** patients with (I) by intravenous infusion at 5 g/m2 at 4 week intervals for 3 months and subsequently at 3 month intervals caused an improvement in the ambulation index in two of the patients and caused no side-effects/

ADVANTAGE - (I) is effective against all types of **multiple sclerosis**, markedly alleviates the disease and is well tolerated (i.e. free of the side-effects of prior art drugs such as mitoxantrone, cyclophosphamide or methotrexate). Direct treatment with (I)/(I') (previously used for conditioning patients before stem cell transplantation) is a safer and simpler alternative to stem cell transplantation.

Dwg.0/18
FS CPI
FA AB; DCN
MC CPI: B10-A09B; **B14-S01**
TECH UPTX: 20040326
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Derivatives: (I') is **busulfan, dimethylbusulfan, pentasulfan** or **hepsulfan**.
ABEX UPTX: 20040326
ADMINISTRATION - (I)/(I') is specifically administered as an infusion solution or oral formulation, at a dose of 1-10 (preferably 5-8) g per m%2 of body surface, optionally in combination with immunomodulator (preferably **interferon** or **glatriamer acetate**) (all claimed).

=> => fil medline
FILE 'MEDLINE' ENTERED AT 15:34:36 ON 28 FEB 2006

FILE LAST UPDATED: 23 FEB 2006 (20060223/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot

L102 ANSWER 1 OF 4 MEDLINE on STN
AN 2004239532 MEDLINE
DN PubMed ID: 14648027
TI Allogeneic hematopoietic stem cell transplantation in a patient affected by large granular lymphocyte leukemia and **multiple sclerosis**.
AU La Nasa Giorgio; Littera Roberto; Cocco Eleonora; Battistini Luca; Marrosu Maria Giovanna; Contu Licinio
CS Centro Trapianti di Midollo Osseo, Centro Regionale Trapianti, Ospedale R. Binaghi ASL n degrees 8, Via Is Guadazzonis, 3, 09126 Cagliari, Italy.. lanasa@tiscalinet.it
SO Annals of hematology, (2004 Jun) Vol. 83, No. 6, pp. 403-5. Electronic Publication: 2003-11-26.
Journal code: 9107334. ISSN: 0939-5555.
CY Germany: Germany, Federal Republic of
DT (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200407
ED Entered STN: 20040513
Last Updated on STN: 20040714
Entered Medline: 20040713
AB We describe a 57-year-old man, affected by large granular lymphocyte (LGL) leukemia and concomitant primary progressive **multiple sclerosis** (MS), treated with allogeneic hematopoietic stem cell transplantation (HSCT) from an HLA-identical sibling. The patient was conditioned with fludarabine, **busulphan**, and cyclophosphamide. Graft-versus-host disease (GVHD) prophylaxis consisted of cyclosporine and short-term methotrexate. At 3 years follow-up, the patient is in complete remission of LGL with a marked improvement in neurological conditions. This is the first case of allogeneic HSCT in a patient with LGL leukemia and concomitant primary progressive MS. Allogeneic HSCT, performed in our patient to cure the lymphoproliferative disorder, improved the clinical course of MS.
CT Check Tags: Male
Follow-Up Studies

*Hematopoietic Stem Cell Transplantation: MT, methods
Humans
Leukemia, T-Cell: CO, complications
Leukemia, T-Cell: PA, pathology
*Leukemia, T-Cell: TH, therapy
Middle Aged
Multiple Sclerosis: CO, complications
Multiple Sclerosis: PA, pathology
***Multiple Sclerosis: TH, therapy**
Transplantation Conditioning: MT, methods
Transplantation, Homologous
Treatment Outcome

L102 ANSWER 2 OF 4 MEDLINE on STN
AN 2003519823 MEDLINE
DN PubMed ID: 14597095
TI Action of **treosulfan** in myelin-oligodendrocyte-glycoprotein-induced experimental autoimmune encephalomyelitis and human lymphocytes.
AU Weissert Robert; Wiendl Heinz; Pfrommer Heike; Storch Maria K; Schreiner Bettina; Barth Silvia; Seifert Thomas; Melms Arthur; Dichgans Johannes; Weller Michael
CS Experimental Neuroimmunology Laboratory, Department of General Neurology, Hertie-Institute for Clinical Brain Research, University of Tubingen, Hoppe-Seyler-Strasse 3, 72076 Tubingen, Germany.. robert.weissert@uni-tuebingen.de
SO Journal of neuroimmunology, (2003 Nov) Vol. 144, No. 1-2, pp. 28-37. Journal code: 8109498. ISSN: 0165-5728.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200403
ED Entered STN: 20031105
Last Updated on STN: 20040303
Entered Medline: 20040302
AB **Treosulfan** (dihydroxybusulfane, DHB, L-threitol-1,4-bis [methane sulfonate]) is a cytostatic alkylating agent with a favorable profile of side effects. Myelin-oligodendrocyte-glycoprotein (MOG)-induced experimental autoimmune encephalomyelitis (EAE) induced in DA (RT1(av1)) rats resembles **multiple sclerosis** (MS) in many aspects since central nervous system (CNS) pathology shows inflammation, demyelination and axonal loss. Moreover, DA rats develop a chronic disease course. We here explored the efficacy of **treosulfan** in the treatment of MOG-induced EAE in DA rats. A single dose of **treosulfan** (1 g/kg body weight i.p.) at the day of immunization significantly reduced disease severity compared with PBS-treated controls. In addition, after disease had evolved, a single dose of **treosulfan** (1 g/kg body weight) given i.p. on day 14 post-immunization (p.i.) improved long-term disease outcome. Treatment with **treosulfan** resulted in reduced mRNA expression of IL-12 and interferon (IFN)-gamma in draining lymph nodes and reduced numbers of IFN-gamma-secreting MOG-specific T cells. No myelosuppression was observed. **Treosulfan** was applied to different subsets of cultured human blood mononuclear cells in order to asses the effects on human immune cells in vitro: **Treosulfan** reduced proliferative capacity and increased apoptosis in T cells and antigen-presenting cells. In light of the beneficial effects in EAE in vivo and the in vitro immunosuppressive and pro-apoptotic capacities in cultured human mononuclear immune effector cells, these data may support a potential role of **treosulfan**, an agent with high immunosuppressive capacity and

low toxicity, in the treatment of MS.
CT Check Tags: Female
Amino Acid Sequence
Animals
Antigen Presentation: DE, drug effects
Antigens, Differentiation, T-Lymphocyte: BI, biosynthesis
Apoptosis: DE, drug effects
Apoptosis: IM, immunology
Bone Marrow Cells: DE, drug effects
***Busulfan: AA, analogs & derivatives**
***Busulfan: TU, therapeutic use**
Busulfan: TO, toxicity
Cell Differentiation: DE, drug effects
Cell Differentiation: IM, immunology
Cytokines: AI, antagonists & inhibitors
Cytokines: BI, biosynthesis
Cytokines: GE, genetics
Dendritic Cells: CY, cytology
Dendritic Cells: DE, drug effects
Dendritic Cells: IM, immunology
Dendritic Cells: ME, metabolism
*Encephalomyelitis, Autoimmune, Experimental: DT, drug therapy
*Encephalomyelitis, Autoimmune, Experimental: IM, immunology
Encephalomyelitis, Autoimmune, Experimental: PA, pathology
Humans
*Immunosuppressive Agents: TU, therapeutic use
Immunosuppressive Agents: TO, toxicity
Injections, Intradermal
Injections, Intraperitoneal
Lymphocyte Activation: DE, drug effects
*Lymphocytes: DE, drug effects
Molecular Sequence Data
Monocytes: CY, cytology
Monocytes: DE, drug effects
Monocytes: IM, immunology
Monocytes: ME, metabolism
*Myelin-Associated Glycoprotein: IM, immunology
RNA, Messenger: AI, antagonists & inhibitors
RNA, Messenger: BI, biosynthesis
Rats
Rats, Inbred Strains
Research Support, Non-U.S. Gov't
T-Lymphocytes: CY, cytology
T-Lymphocytes: DE, drug effects
T-Lymphocytes: IM, immunology
RN **299-75-2 (treosulfan); 55-98-1 (Busulfan)**
CN 0 (Antigens, Differentiation, T-Lymphocyte); 0 (Cytokines); 0 (Immunosuppressive Agents); 0 (Myelin-Associated Glycoprotein); 0 (RNA, Messenger); 0 (oligodendrocyte-myelin glycoprotein)

L102 ANSWER 3 OF 4 MEDLINE on STN
AN 2000512761 MEDLINE
DN PubMed ID: 11071262
TI Peripheral blood stem cell transplantation in **multiple sclerosis** with **busulfan** and cyclophosphamide conditioning: report of toxicity and immunological monitoring.
AU Openshaw H; Lund B T; Kashyap A; Atkinson R; Sniecinski I; Weiner L P; Forman S
CS Department of Neurology, City of Hope National Medical Center, Duarte, California 91010, USA.. hopenshaw@coh.org

NC CA 30206 (NCI)
CA 33572 (NCI)
SO Biology of blood and marrow transplantation : journal of the American Society for Blood and Marrow Transplantation, (2000) Vol. 6, No. 5A, pp. 563-75.
Journal code: 9600628. ISSN: 1083-8791.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010308
AB **Multiple sclerosis** (MS) is an immune-mediated disease that may be amenable to high-dose immunosuppression with peripheral blood stem cell transplantation (SCT) in selected patients. Five MS patients (all women, ages 39-47 years) received granulocyte colony-stimulating factor (G-CSF) for stem cell mobilization, CD34 cell selection for T-cell depletion, a preparatory regimen of **busulfan** (1 mg/kg x 16 doses) and cyclophosphamide (120 mg/kg), and antithymocyte globulin (10 mg/kg x 3 doses) at the time of stem cell infusion. Days required to recover absolute neutrophil count >500 were 12 to 14 and platelet count >20,000 were 17 to 58. Posttransplantation infectious complications in the first year after SCT occurred in 3 of 5 patients, and 1 patient died at day 22 after SCT from influenza A pneumonia. Neuropathologic study in this patient showed demyelinating plaques with surrounding macrophages but only rare T cells. In 2 patients, MS flared transiently with G-CSF. Magnetic resonance imaging gadolinium enhancement was present in 3 of 5 patients before transplantation and 0 of 4 after SCT. There were cerebrospinal fluid oligoclonal bands at 1 year after SCT, similar to the pretransplantation assays. Sustained suppression of peripheral blood mononuclear cell proliferative responses to myelin antigens occurred after SCT, but new responses to some myelin peptide fragments also developed after SCT. In 1 patient, enzyme-linked immunospot (ELISPOT) assays done 9 months after SCT showed a predominant T helper 2 (Th2) cytokine pattern. Neurological progression of 1 point on the extended disability status scale was seen in 1 patient 17 months after SCT. Another patient who was neurologically stable died abruptly 19 months after SCT from overwhelming S. pneumoniae sepsis. The remaining patients have had stable MS (follow-up, 18 and 30 months). In summary, our experience confirms the high-risk nature of this approach. Further studies and longer follow-up would be needed to determine the significance of new lymphocyte proliferative responses after SCT and the overall effect of this treatment on the natural history of MS.
CT Check Tags: Female
Adult
Autoantibodies: IM, immunology
Autoantigens: IM, immunology
Autoimmune Diseases: CF, cerebrospinal fluid
Autoimmune Diseases: IM, immunology
Autoimmune Diseases: PA, pathology
*Autoimmune Diseases: TH, therapy
Brain: PA, pathology
***Busulfan: AD, administration & dosage**
Busulfan: AE, adverse effects
Cells, Cultured
Combined Modality Therapy
*Cyclophosphamide: AD, administration & dosage
Cyclophosphamide: AE, adverse effects

Cytotoxicity, Immunologic
Disease Progression
Granulocyte Colony-Stimulating Factor: AE, adverse effects
Granulocyte Colony-Stimulating Factor: PD, pharmacology
Hematopoietic Stem Cell Mobilization
*Hematopoietic Stem Cell Transplantation
Hematopoietic Stem Cell Transplantation: AE, adverse effects
Humans
Immunodominant Epitopes: IM, immunology
Immunosuppression
Immunosuppressive Agents: TU, therapeutic use
Infection: ET, etiology
Infection: MO, mortality
Lymphocyte Activation
Magnetic Resonance Imaging
Methylprednisolone: TU, therapeutic use
Middle Aged
Multiple Sclerosis: CF, cerebrospinal fluid
Multiple Sclerosis: IM, immunology
Multiple Sclerosis: PA, pathology
***Multiple Sclerosis: TH, therapy**
Myelin Sheath: IM, immunology
Research Support, U.S. Gov't, P.H.S.
T-Lymphocyte Subsets: IM, immunology
*Transplantation Conditioning
Transplantation Conditioning: AE, adverse effects
Treatment Outcome

RN 143011-72-7 (Granulocyte Colony-Stimulating Factor); 50-18-0 (Cyclophosphamide); **55-98-1 (Busulfan)**; 83-43-2 (Methylprednisolone)
CN 0 (Autoantibodies); 0 (Autoantigens); 0 (Immunodominant Epitopes); 0 (Immunosuppressive Agents)

L102 ANSWER 4 OF 4 MEDLINE on STN
AN 96421865 MEDLINE
DN PubMed ID: 8824482
TI Treatment of relapsing experimental autoimmune encephalomyelitis with largely MHC-matched allogeneic bone marrow transplantation.
AU van Gelder M; Mulder A H; van Bekkum D W
CS Introgene B.V., Rijswijk, The Netherlands.
SO Transplantation, (1996 Sep 27) Vol. 62, No. 6, pp. 810-8.
Journal code: 0132144. ISSN: 0041-1337.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199612
ED Entered STN: 19970128
Last Updated on STN: 20000303
Entered Medline: 19961210
AB BUF rats suffering from severe relapsing experimental autoimmune encephalomyelitis (R-EAE), a model for **multiple sclerosis**, were treated with intensive cytoreductive therapy and grafting of allogeneic bone marrow (BM). BN.1B rats were used as EAE-resistant, largely MHC-matched donors, resembling human BMT from HLA-identical siblings. The treatment induces complete remission and low recurrence rates of R-EAE. Evidence is provided that the efficacy of the treatment depends on a high degree of lymphoablation: a minority of rats had host-type residual activated T lymphocytes in the CNS after treatment. Furthermore, complete replacement of host-type BM by donor-type

hemopoietic cells is essential, as higher relapse rates were observed in animals with incomplete reconstitution by donor cells than in completely reconstituted rats. Overall, our results indicate that patients with severe MS might benefit from treatment with HLA-matched allogeneic BM.

CT Animals
Antibodies, Monoclonal: IM, immunology
Antibodies, Monoclonal: PD, pharmacology
*Bone Marrow Transplantation
Busulfan
Cyclophosphamide
Disease Models, Animal
*Encephalomyelitis, Autoimmune, Experimental: TH, therapy
Graft vs Host Reaction
Histocompatibility
*Histocompatibility Antigens: IM, immunology
Lymphocyte Depletion
Multiple Sclerosis
Radiation Chimera
Rats
Rats, Inbred BN
Rats, Inbred BUF
Recurrence
Remission Induction
Research Support, Non-U.S. Gov't
T-Lymphocytes, Cytotoxic: IM, immunology
Transplantation Conditioning
Transplantation, Homologous
Whole-Body Irradiation

RN 50-18-0 (Cyclophosphamide); **55-98-1 (Busulfan)**

CN 0 (Antibodies, Monoclonal); 0 (Histocompatibility Antigens); 0 (histocompatibility antigens RT, rat)

=> => fil embase
FILE 'EMBASE' ENTERED AT 15:41:38 ON 28 FEB 2006

FILE COVERS 1974 TO 24 Feb 2006 (20060224/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l126 all tot

L126 ANSWER 1 OF 10 EMBASE
AN 2004370458 EMBASE
TI **Multiple sclerosis.**
AU Fassas A.; Nash R.
CS A. Fassas, Bone Marrow Transplantation Unit, Department of Haematology, George Papanicolaou Hospital, 57010 Exokhi, Thessaloniki, Greece. hempap@otenet.gr
SO Best Practice and Research in Clinical Haematology, (2004) Vol. 17, No. 2, pp. 247-262. .
Refs: 72
ISSN: 1521-6926 CODEN: BPRCA5
PUI S 1521-6926(04)00018-0
CY United Kingdom

DT Journal; General Review
FS 005 General Pathology and Pathological Anatomy
025 Hematology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
052 Toxicology
LA English
SL English
ED Entered STN: 20040916
Last Updated on STN: 20040916
AB Autologous transplants for severe and refractory **multiple sclerosis** (MS) were proposed in 1997 and have been performed on about 200 selected patients worldwide. Phase I/II clinical studies have shown that high-dose immunosuppressive therapy suppresses inflammation in the CNS and may delay the progression of clinical disease. The procedure is associated with toxicity from the high-dose cytotoxic therapy and a risk of serious infections. There is a transplant-related mortality risk of 1-5%, requiring careful patient selection before transplantation. Treatment should be reserved for patients who have a significant chance of response, i.e. young patients with low disability scores but rapidly progressing disease who have inflammatory rather than neurodegenerative changes in the CNS. The long term effect of high-dose immunosuppression after transplantation on the frequency of relapse or progression of MS is unclear, but the initial concept of immune ablation by high-dose therapy and the reconstitution of normal immunity and tolerance from transplant-derived lymphocyte progenitors has given way to the concept of 'resetting' the immune system. The clinical effect of transplantation remains to be demonstrated in comparative studies.
CT Medical Descriptors:
***multiple sclerosis: DI, diagnosis**
***multiple sclerosis: DR, drug resistance**
***multiple sclerosis: DT, drug therapy**
***multiple sclerosis: ET, etiology**
***multiple sclerosis: RT, radiotherapy**
***multiple sclerosis: TH, therapy**
*autologous hematopoietic stem cell transplantation
disease severity
immunosuppressive treatment
drug megadose
central nervous system disease: DT, drug therapy
disease course
infection risk
mortality
patient selection
drug response
scoring system
degenerative disease: DI, diagnosis
degenerative disease: DR, drug resistance
degenerative disease: DT, drug therapy
degenerative disease: ET, etiology
degenerative disease: RT, radiotherapy
degenerative disease: TH, therapy
recurrence risk
immunological tolerance
lymphocyte
bacterial infection: SI, side effect
mycosis: SI, side effect
virus infection: SI, side effect

cardiotoxicity: SI, side effect
hemophilia: SI, side effect
drug fatality: SI, side effect
influenza: SI, side effect
Streptococcus infection: SI, side effect
disease exacerbation: SI, side effect
Herpes virus infection: SI, side effect
lymphoma: SI, side effect
liver vein obstruction: SI, side effect
peripheral blood stem cell transplantation
urinary tract infection: SI, side effect
cytomegalovirus infection: SI, side effect
lymphoproliferative disease: SI, side effect
drug eruption: SI, side effect
drug fever: SI, side effect
neurologic disease: SI, side effect
lower respiratory tract infection: SI, side effect
human
nonhuman
clinical trial
phase 1 clinical trial
phase 2 clinical trial
review
priority journal
Drug Descriptors:
immunosuppressive agent: AE, adverse drug reaction
immunosuppressive agent: CT, clinical trial
immunosuppressive agent: CB, drug combination
immunosuppressive agent: DO, drug dose
immunosuppressive agent: DT, drug therapy
immunosuppressive agent: TO, drug toxicity
cytotoxic agent: AE, adverse drug reaction
cytotoxic agent: CT, clinical trial
cytotoxic agent: CB, drug combination
cytotoxic agent: DO, drug dose
cytotoxic agent: DT, drug therapy
cytotoxic agent: TO, drug toxicity
glucocorticoid: DT, drug therapy
immunomodulating agent: DT, drug therapy
immunoglobulin: DT, drug therapy
immunoglobulin: IV, intravenous drug administration
monoclonal antibody: DT, drug therapy
corticosteroid: DT, drug therapy
beta interferon: AE, adverse drug reaction
beta interferon: DT, drug therapy
glatiramer: DT, drug therapy
mitoxantrone: CT, clinical trial
mitoxantrone: CB, drug combination
mitoxantrone: DT, drug therapy
cyclophosphamide: AE, adverse drug reaction
cyclophosphamide: CT, clinical trial
cyclophosphamide: CB, drug combination
cyclophosphamide: DO, drug dose
cyclophosphamide: DT, drug therapy
busulfan: AE, adverse drug reaction
busulfan: CT, clinical trial
busulfan: CB, drug combination
busulfan: DO, drug dose
busulfan: DT, drug therapy
busulfan: TO, drug toxicity

granulocyte colony stimulating factor: CT, clinical trial
granulocyte colony stimulating factor: CB, drug combination
thymocyte antibody: AE, adverse drug reaction
thymocyte antibody: CT, clinical trial
thymocyte antibody: CB, drug combination
thymocyte antibody: DO, drug dose
thymocyte antibody: DT, drug therapy
gadolinium
carmustine: AE, adverse drug reaction
carmustine: CT, clinical trial
carmustine: CB, drug combination
carmustine: DT, drug therapy
etoposide: AE, adverse drug reaction
etoposide: CT, clinical trial
etoposide: CB, drug combination
etoposide: DT, drug therapy
cytarabine: AE, adverse drug reaction
cytarabine: CT, clinical trial
cytarabine: CB, drug combination
cytarabine: DT, drug therapy
melphalan: AE, adverse drug reaction
melphalan: CT, clinical trial
melphalan: CB, drug combination
melphalan: DT, drug therapy
granulocyte macrophage colony stimulating factor: CT, clinical trial
granulocyte macrophage colony stimulating factor: CB, drug combination
prednisone: CT, clinical trial
prednisone: CB, drug combination

CT Drug Descriptors:
prednisone: DT, drug therapy
dexamethasone: CT, clinical trial
dexamethasone: CB, drug combination
dexamethasone: DT, drug therapy
cladribine: DT, drug therapy
alemtuzumab: DT, drug therapy

RN (immunoglobulin) 9007-83-4; (glatiramer) **147245-92-9**, **28704-27-0**; (mitoxantrone) 65271-80-9, 70476-82-3; (cyclophosphamide) 50-18-0; (**busulfan**) **55-98-1**; (gadolinium) 7440-54-2; (carmustine) 154-93-8; (etoposide) 33419-42-0; (cytarabine) 147-94-4, 69-74-9; (melphalan) 148-82-3; (prednisone) 53-03-2; (dexamethasone) 50-02-2; (cladribine) 4291-63-8; (alemtuzumab) 216503-57-0

CN Decadron

L126 ANSWER 2 OF 10 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

AN 2004284056 EMBASE

TI [**Multiple sclerosis**: Potential therapeutic options and update of ongoing clinical trials].
MULTIPLE SKLEROSE: POTENZIELLE THERAPIEANSATZE UND UPDATE LAUFENDER STUDIEN.

AU Wiendl H.; Lehmann H.C.; Hohlfeld R.; Hartung H.-P.; Kieseier B.C.

CS Dr. H. Wiendl, Abt. fur Allg. Neurologie und Hertie, Institut Klinische Hirnforschung, Universitat Tubingen, Hoppe-Seyler-Strasse 3, 72076 Tubingen, Germany. heinz.wiendl@uni-tuebingen.de

SO Nervenarzt, (2004) Vol. 75, No. 6, pp. 536-552. .
Refs: 138
ISSN: 0028-2804 CODEN: NERVAF

CY Germany

DT Journal; General Review

FS 008 Neurology and Neurosurgery
037 Drug Literature Index
LA German
SL English; German
ED Entered STN: 20040722
Last Updated on STN: 20040722
AB The therapeutic options for the treatment of **multiple sclerosis** (MS) have experienced enormous progress over recent years. Despite these encouraging developments, available therapies are only partially effective, and the ultimate goal of curing MS is still far from being attained. The improved understanding of the cellular and molecular mechanisms of MS (immune) pathogenesis together with recent shifts in paradigms led to a variety of new therapeutic targets and approaches. In addition to modulation of the inflammatory process, therapeutic approaches focussing on active neuroprotection, remyelinization, and regeneration have become increasingly important. Based on current concepts of the MS pathogenesis, this article summarizes new therapeutic approaches. Substances and strategies currently tested in clinical trials are reviewed.
CT Medical Descriptors:
***multiple sclerosis: DT, drug therapy**
***multiple sclerosis: ET, etiology**
***multiple sclerosis: TH, therapy**
inflammation
neuroprotection
remyelinization
nerve regeneration
stem cell transplantation
immunomodulation
human
major clinical study
clinical trial
controlled study
review
Drug Descriptors:
alemtuzumab: CT, clinical trial
alemtuzumab: DT, drug therapy
rituximab: CT, clinical trial
rituximab: DT, drug therapy
natalizumab: CT, clinical trial
natalizumab: DO, drug dose
natalizumab: DT, drug therapy
natalizumab: IV, intravenous drug administration
riluzole: CT, clinical trial
riluzole: DT, drug therapy
rapamycin: CT, clinical trial
rapamycin: DT, drug therapy
xaliproden: CT, clinical trial
xaliproden: DT, drug therapy
xaliproden: PO, oral drug administration
teriflunomide: CT, clinical trial
teriflunomide: DO, drug dose
teriflunomide: DT, drug therapy
teriflunomide: PO, oral drug administration
mycophenolic acid 2 morpholinoethyl ester: CT, clinical trial
mycophenolic acid 2 morpholinoethyl ester: DT, drug therapy
treosulfan: CT, clinical trial
treosulfan: DT, drug therapy
valaciclovir: CT, clinical trial
valaciclovir: DT, drug therapy

daclizumab: CT, clinical trial
daclizumab: DT, drug therapy
minocycline: CT, clinical trial
minocycline: DT, drug therapy
2 amino 2 [2 (4 octylphenyl)ethyl] 1,3 propanediol: CT, clinical trial
2 amino 2 [2 (4 octylphenyl)ethyl] 1,3 propanediol: DT, drug therapy
2 amino 2 [2 (4 octylphenyl)ethyl] 1,3 propanediol: PD, pharmacology
razoxane: DT, drug therapy
mitoxantrone: DT, drug therapy
azathioprine: DT, drug therapy
rapamycin 2,2 bis(hydroxymethyl)propionate: CT, clinical trial
rapamycin 2,2 bis(hydroxymethyl)propionate: DT, drug therapy
rapamycin 2,2 bis(hydroxymethyl)propionate: PO, oral drug administration
rifampicin: CT, clinical trial
rifampicin: CB, drug combination
rifampicin: DT, drug therapy
azithromycin: CT, clinical trial
azithromycin: CB, drug combination
azithromycin: DT, drug therapy
immunoglobulin G1 antibody: CT, clinical trial
immunoglobulin G1 antibody: DT, drug therapy
atm 027: CT, clinical trial
atm 027: DT, drug therapy
CD40 ligand monoclonal antibody: CT, clinical trial
CD40 ligand monoclonal antibody: DT, drug therapy
idec 131: CT, clinical trial
idec 131: DT, drug therapy
interleukin 2 receptor antibody
cytotoxic T lymphocyte antigen 4: CT, clinical trial
cytotoxic T lymphocyte antigen 4: DO, drug dose
cytotoxic T lymphocyte antigen 4: DT, drug therapy
cytotoxic T lymphocyte antigen 4: IV, intravenous drug administration
placebo
T lymphocyte receptor: CT, clinical trial
T lymphocyte receptor: DT, drug therapy
thalidomide: DT, drug therapy
pentoxifylline: DT, drug therapy
unindexed drug
unclassified drug
bbr 2778
neurovax
laquinimod
bx 471
cep 1s1
hmr 1726
simvastatin
leflunomide
testosterone
ir 208
glatiramer

RN (alemtuzumab) 216503-57-0; (rituximab) 174722-31-7; (natalizumab) 189261-10-7; (riluzole) 1744-22-5; (rapamycin) 53123-88-9; (xaliproden) 90494-79-4; (teriflunomide) 108605-62-5; (mycophenolic acid 2 morpholinoethyl ester) 116680-01-4, 128794-94-5; (**treosulfan**) **21106-06-9, 299-75-2**; (valaciclovir) 124832-26-4; (minocycline) 10118-90-8, 11006-27-2, 13614-98-7; (2 amino 2 [2 (4 octylphenyl)ethyl] 1,3 propanediol) 162359-56-0; (razoxane) 21416-67-1, 21416-87-5, 24584-09-6, 24613-06-7; (mitoxantrone) 65271-80-9, 70476-82-3; (azathioprine) 446-86-6; (rapamycin 2,2 bis(hydroxymethyl)propionate) 162635-04-3, 343261-52-9; (rifampicin) 13292-46-1; (azithromycin)

83905-01-5; (interleukin 2 receptor antibody) 179045-86-4; (thalidomide) 50-35-1; (pentoxifylline) 6493-05-6; (simvastatin) 79902-63-9; (leflunomide) 75706-12-6; (testosterone) 58-22-0; (glatiramer) **147245-92-9, 28704-27-0**

CN (1) Zenapax; (2) Fty 720; (3) Bbr 2778; (4) Atm 027; (5) Bms 188667; (6) Idec 131; (7) Alemtuzumab; (8) Neurovax; (9) Mabthera; (10) Antegren; (11) Cellcept; (12) Abr 215062; (13) Cci 779; (14) Rituxan; (15) Bx 471; (16) Cep 1s1; (17) Rapamune; (18) Hmr 1726; (19) Zocor; (20) Valtrex; Rilutek; Zinecard; Ovastat; Arava; Androgel; Ir 208; **Copaxone**

CO (2) Novartis; (3) Novuspharma; (4) AVANT; (5) Bristol Myers Squibb; (6) Idec; (7) Millennium Pharmaceuticals; (8) Immune Response; (10) Elan; (11) Hoffmann La Roche; (12) Active Biotech; (14) Genentech; (15) Berlex; (16) Cephalon; (17) Wyeth; (18) Aventis; (19) Merck and Co; (20) Glaxo SmithKline; Sanofi Synthelabo; Medac

L126 ANSWER 3 OF 10 EMBASE

AN 2003446229 EMBASE

TI Stem cell transplantation for **multiple sclerosis**: What is the evidence?.

AU Fassas A.; Kimiskidis V.K.

CS Dr. A. Fassas, Hematology Department, BMT Unit, George Papanicolaou Hospital, Exokhi, Thessaloniki 57010, Greece. hempap@otenet.gr

SO Blood Reviews, (2003) Vol. 17, No. 4, pp. 233-240. .
Refs: 72
ISSN: 0268-960X CODEN: BLOREB

CY United Kingdom

DT Journal; General Review

FS 008 Neurology and Neurosurgery
025 Hematology
037 Drug Literature Index
038 Adverse Reactions Titles

LA English

SL English

ED Entered STN: 20031120
Last Updated on STN: 20031120

AB Experimental and clinical observations have indicated that high-dose immunosuppression followed by autologous stem cell transplantation (ASCT) can induce remissions in severe, refractory, autoimmune diseases including **multiple sclerosis** (MS), a T cell-mediated autoimmune disorder against CNS myelin components, causing severe chronic disability. Control of the disease is unsatisfactory in most of the patients, especially those with rapidly evolving relapsing-remitting course and those with chronic progressive disease. The rationale for treating autoimmune diseases with ASCT is based on the immunosuppressive and immunomodulating effects of ASCT which may shift the immunological balance towards disease quiescence, a hypothesis supported by the results of ASCT in animal models of MS and by clinical observations in MS patients transplanted for concurrent malignancies. A number of phase I-II studies of ASCT in patients with active MS, conducted worldwide since 1995, and a comprehensive analysis of 85 patients, recently reported by the European Group for Blood and Marrow Transplantation (EBMT), have shown the feasibility of the method, a prominent anti-inflammatory effect on magnetic resonance imaging (MRI) disease, and a possible clinical benefit for active and refractory cases. The impact on MRI disease parameters appears superior with ASCT than with conventional therapies but the clinical results, in terms of stabilization of disease and prevention of disability, need to be validated in prospective, controlled trials. The procedure is also associated with a transplant-related mortality risk, of about 5% in high-risk cases, i.e., in older patients, those with high

disability scores, those receiving strong myeloablative conditioning regimens and those undergoing intensive in vivo or ex vivo T cell-depletion. Therefore, it could be recommended for the treatment of a chronic, non-lethal, disease like MS only if it proved superior to standard therapies. A randomized trial is now launched by the EBMT to compare ASCT to mitoxantrone, currently regarded as one of the best available treatments, in properly selected patients having high chance of response at minimal mortality risk.

CT Medical Descriptors:
***multiple sclerosis: DT, drug therapy**
***multiple sclerosis: TH, therapy**
*stem cell transplantation
immunosuppressive treatment
autotransplantation
remission
immunomodulation
feasibility study
nuclear magnetic resonance imaging
antiinflammatory activity
mortality
high risk patient
age
disability
neurologic disease: SI, side effect
disease exacerbation: SI, side effect
bleeding
human
nonhuman
male
female
clinical trial
phase 1 clinical trial
phase 2 clinical trial
aged
adult
review
priority journal
Drug Descriptors:
*immunosuppressive agent: DT, drug therapy
mitoxantrone: DT, drug therapy
steroid: DT, drug therapy
cytotoxic agent: DT, drug therapy
beta interferon: AE, adverse drug reaction
beta interferon: DT, drug therapy
glatiramer: DT, drug therapy
immunoglobulin: DT, drug therapy
immunoglobulin: IV, intravenous drug administration
carmustine: CB, drug combination
etoposide: CB, drug combination
cytarabine: CB, drug combination
cytarabine: DO, drug dose
melphalan: CB, drug combination
busulfan: DO, drug dose
fludarabine: CB, drug combination
thymocyte antibody: CB, drug combination
granulocyte colony stimulating factor: AE, adverse drug reaction
granulocyte colony stimulating factor: DT, drug therapy
alemtuzumab: AE, adverse drug reaction
alemtuzumab: DT, drug therapy

CD34 antigen
RN (mitoxantrone) 65271-80-9, 70476-82-3; (glatiramer) **147245-92-9**, **28704-27-0**; (immunoglobulin) 9007-83-4; (carmustine) 154-93-8; (etoposide) 33419-42-0; (cytarabine) 147-94-4, 69-74-9; (melphalan) 148-82-3; (**busulfan**) **55-98-1**; (fludarabine) 21679-14-1; (alemtuzumab) 216503-57-0

L126 ANSWER 4 OF 10 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
AN 2003438369 EMBASE
TI Action of **treosulfan** in myelin-oligodendrocyte-glycoprotein-induced experimental autoimmune encephalomyelitis and human lymphocytes.
AU Weissert R.; Wiendl H.; Pfrommer H.; Storch M.K.; Schreiner B.; Barth S.; Seifert T.; Melms A.; Dichgans J.; Weller M.
CS R. Weissert, Department of General Neurology, Hertie-Inst. for Clin. Brain Res., University of Tubingen, Hoppe-Seyler-Strasse 3, 72076 TTubingenbingen, Germany. robert.weissert@uni-tuebingen.de
SO Journal of Neuroimmunology, (2003) Vol. 144, No. 1-2, pp. 28-37. .
Refs: 36
ISSN: 0165-5728 CODEN: JNRIDW
Nov 2003
CY Netherlands
DT Journal; Article
FS 008 Neurology and Neurosurgery
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
052 Toxicology
LA English
SL English
ED Entered STN: 20031120
Last Updated on STN: 20031120
AB **Treosulfan** (dihydroxybusulfane, DHB, L-threitol-1,4-bis [methane sulfonate]) is a cytostatic alkylating agent with a favorable profile of side effects. Myelin-oligodendrocyte-glycoprotein (MOG)-induced experimental autoimmune encephalomyelitis (EAE) induced in DA (RT1(av1)) rats resembles **multiple sclerosis** (MS) in many aspects since central nervous system (CNS) pathology shows inflammation, demyelination and axonal loss. Moreover, DA rats develop a chronic disease course. We here explored the efficacy of **treosulfan** in the treatment of MOG-induced EAE in DA rats. A single dose of **treosulfan** (1 g/kg body weight i.p.) at the day of immunization significantly reduced disease severity compared with PBS-treated controls. In addition, after disease had evolved, a single dose of **treosulfan** (1 g/kg body weight) given i.p. on day 14 post-immunization (p.i.) improved long-term disease outcome. Treatment with **treosulfan** resulted in reduced mRNA expression of IL-12 and interferon (IFN)-γ in draining lymph nodes and reduced numbers of IFN-γ-secreting MOG-specific T cells. No myelosuppression was observed. **Treosulfan** was applied to different subsets of cultured human blood mononuclear cells in order to asses the effects on human immune cells in vitro: **Treosulfan** reduced proliferative capacity and increased apoptosis in T cells and antigen-presenting cells. In light of the beneficial effects in EAE in vivo and the in vitro immunosuppressive and pro-apoptotic capacities in cultured human mononuclear immune effector cells, these data may support a potential role of **treosulfan**, an agent with high immunosuppressive capacity and low toxicity, in the treatment of MS. .COPYRGT. 2003 Elsevier B.V. All rights reserved.
CT Medical Descriptors:
*allergic encephalomyelitis: DT, drug therapy

*lymphocyte
drug efficacy
immunization
disease severity
disease duration
treatment outcome
drug effect
lymph node
cytokine release
T lymphocyte
mononuclear cell
cell subpopulation
immunocompetent cell
in vitro study
apoptosis
lymphocyte proliferation
antigen presenting cell
effector cell
bone marrow toxicity
nonhuman
female
rat
animal experiment
animal model
controlled study
animal tissue
animal cell
article
priority journal
Drug Descriptors:
***treosulfan: DT, drug therapy**
***treosulfan: TO, drug toxicity**
***treosulfan: PD, pharmacology**
***treosulfan: IP, intraperitoneal drug administration**
*myelin oligodendrocyte glycoprotein
messenger RNA: EC, endogenous compound
interleukin 12: EC, endogenous compound
gamma interferon: EC, endogenous compound
immunosuppressive agent: DT, drug therapy
immunosuppressive agent: TO, drug toxicity
immunosuppressive agent: PD, pharmacology
immunosuppressive agent: IP, intraperitoneal drug administration
RN (**treosulfan**) **21106-06-9, 299-75-2;**
(interleukin 12) 138415-13-1; (gamma interferon) 82115-62-6
CN (1) Ovastat
CO (1) Medac (Germany)

L126 ANSWER 5 OF 10 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
AN 2003356698 EMBASE
TI Hematopoietic stem cell transplantation for **multiple sclerosis**: Finding equipoise.
AU Burt R.K.; Kozak T.
CS Dr. R.K. Burt, Northwestern Univ. Medical Center, 320 East Superior, Searle 3-489, Chicago, IL 60611, United States. rburt@nwu.edu
SO Bone Marrow Transplantation, (2003) Vol. 32, No. SUPPL. 1, pp. S45-S48. .
Refs: 34
ISSN: 0268-3369 CODEN: BMTRE
CY United Kingdom
DT Journal; Article

FS 008 Neurology and Neurosurgery
014 Radiology
025 Hematology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
ED Entered STN: 20030918
Last Updated on STN: 20030918
AB Hematopoietic stem cell transplantation of **multiple sclerosis** is rapidly expanding. Success for this approach requires an understanding of the pathophysiology of **multiple sclerosis** and design of trials that select patients with active inflammatory disease, low disability scores, and avoidance of conditioning agents that may damage neural stem cell compartments or further compromise already injured axons.
CT Medical Descriptors:
***multiple sclerosis: DT, drug therapy**
***multiple sclerosis: RT, radiotherapy**
***multiple sclerosis: TH, therapy**
hematopoietic stem cell transplantation
treatment outcome
pathophysiology
patient selection
inflammation
scoring system
cell compartmentalization
nerve cell
axonal injury
dose response
immunosuppressive treatment
lymphocyte depletion
opportunistic infection: CO, complication
opportunistic infection: SI, side effect
aspergillosis: CO, complication
aspergillosis: SI, side effect
sepsis: SI, side effect
Streptococcus infection: SI, side effect
stem cell mobilization
lymphoproliferative disease: CO, complication
lymphoproliferative disease: SI, side effect
peripheral blood stem cell
female infertility: CO, complication
female infertility: SI, side effect
whole body radiation
myelodysplastic syndrome: CO, complication
leukemia: CO, complication
hypothyroidism: CO, complication
cataract: CO, complication
human
clinical trial
article
priority journal
Drug Descriptors:
beta interferon: DT, drug therapy
glatiramer: DT, drug therapy
corticosteroid: DT, drug therapy
corticosteroid: IV, intravenous drug administration
corticosteroid: PO, oral drug administration
cyclophosphamide: AE, adverse drug reaction

cyclophosphamide: CT, clinical trial
cyclophosphamide: CB, drug combination
cyclophosphamide: DT, drug therapy
cyclophosphamide: IV, intravenous drug administration
cyclophosphamide: PO, oral drug administration
azathioprine: DT, drug therapy
mitoxantrone: DT, drug therapy
busulfan: AE, adverse drug reaction
busulfan: CT, clinical trial
busulfan: CB, drug combination
busulfan: DT, drug therapy
thymocyte antibody: AE, adverse drug reaction
thymocyte antibody: CT, clinical trial
thymocyte antibody: CB, drug combination
thymocyte antibody: DT, drug therapy
carmustine: AE, adverse drug reaction
carmustine: CT, clinical trial
carmustine: CB, drug combination
carmustine: DO, drug dose
carmustine: DT, drug therapy
carmustine: IV, intravenous drug administration
etoposide: AE, adverse drug reaction
etoposide: CT, clinical trial
etoposide: CB, drug combination
etoposide: DO, drug dose
etoposide: DT, drug therapy
etoposide: IV, intravenous drug administration
cytarabine: AE, adverse drug reaction
cytarabine: CT, clinical trial
cytarabine: CB, drug combination
cytarabine: DO, drug dose
cytarabine: DT, drug therapy
cytarabine: IV, intravenous drug administration
melphalan: AE, adverse drug reaction
melphalan: CT, clinical trial
melphalan: CB, drug combination
melphalan: DO, drug dose
melphalan: DT, drug therapy
melphalan: IV, intravenous drug administration
granulocyte colony stimulating factor: DT, drug therapy
avenox
interferon beta serine

RN (glatiramer) **147245-92-9, 28704-27-0;**
(cyclophosphamide) 50-18-0; (azathioprine) 446-86-6; (mitoxantrone) 65271-80-9, 70476-82-3; (**busulfan**) **55-98-1;**
(carmustine) 154-93-8; (etoposide) 33419-42-0; (cytarabine) 147-94-4, 69-74-9; (melphalan) 148-82-3; (**interferon** beta serine) 90598-63-3

CN Avenox; Betaseron; **Copaxone**

L126 ANSWER 6 OF 10 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

AN 2003232092 EMBASE

TI Hematopoietic stem cell transplantation for **multiple sclerosis**: Current status and future challenges.

AU Muraro P.A.; Ingoni R.C.; Martin R.

CS R. Martin, Neuroimmunology Branch, Natl. Inst. of Neurol. Dis./Stroke, Building 10, 10 Center Drive, Bethesda, MD 20892-1400, United States. martinr@ninds.nih.gov

SO Current Opinion in Neurology, (2003) Vol. 16, No. 3, pp. 299-305. .

Refs: 72
ISSN: 1350-7540 CODEN: CONEEX
CY United Kingdom
DT Journal; General Review
FS 008 Neurology and Neurosurgery
025 Hematology
037 Drug Literature Index
LA English
SL English
ED Entered STN: 20030626
Last Updated on STN: 20030626
AB Purpose of review: This article reviews recent advances in clinical trials of hematopoietic stem cell transplantation as a therapy for **multiple sclerosis**, and progress in exploring the potential for neural repair of hematopoietic-derived precursors. Recent findings: Important recent findings are that hematopoietic stem cell transplantation can completely suppress the inflammatory component of **multiple sclerosis**, hematopoietic stem cells can migrate into the central nervous systems of rodents and humans, and can differentiate into cells expressing neural and glial markers. Hematopoietic stem cells also have neural and myelin repair potential. The heterogeneity of transplant regimens, the selection of patients at different stages of disease in clinical trials, and the limited duration of follow-up all currently preclude the evaluation of the long-term clinical benefits of hematopoietic stem cell transplantation for **multiple sclerosis**. Summary: Hematopoietic stem cell transplantation is an experimental treatment that shows strong effects on the inflammatory component of **multiple sclerosis**. On the basis of experience acquired from initial pilot studies, controlled clinical trials are now being designed to verify long-term clinical efficacy. Selecting patients at high risk in the earlier stages of the disease that is dominated by inflammation, and monitoring objectively disease activity by magnetic resonance imaging will be critically important in these studies. Recent advances on the migratory potential and on the differentiation plasticity of hematopoietic stem cells have opened new opportunities for remyelination and axonal repair strategies for **multiple sclerosis**. .COPYRGT. 2003 Lippincott Williams & Wilkins.
CT Medical Descriptors:
*hematopoietic stem cell transplantation
***multiple sclerosis: DT, drug therapy**
***multiple sclerosis: TH, therapy**
hematopoietic stem cell
cell migration
central nervous system
cell differentiation
nerve regeneration
cell heterogeneity
disease activity
nuclear magnetic resonance imaging
human
clinical trial
review
Drug Descriptors:
myelin
beta interferon: DT, drug therapy
glatiramer: DT, drug therapy
mitoxantrone: DT, drug therapy
thymocyte antibody
gadolinium

cyclophosphamide: DT, drug therapy
carmustine: DT, drug therapy
etoposide: DT, drug therapy
cytarabine: DT, drug therapy
melphalan: DT, drug therapy
busulfan: DT, drug therapy
granulocyte colony stimulating factor: DT, drug therapy
granulocyte macrophage colony stimulating factor: DT, drug therapy
betala interferon: CT, clinical trial
betala interferon: DT, drug therapy
interferon beta serine: CT, clinical trial
interferon beta serine: DT, drug therapy
RN (glatiramer) **147245-92-9, 28704-27-0**; (mitoxantrone) 65271-80-9, 70476-82-3; (gadolinium) 7440-54-2; (cyclophosphamide) 50-18-0; (carmustine) 154-93-8; (etoposide) 33419-42-0; (cytarabine) 147-94-4, 69-74-9; (melphalan) 148-82-3; (**busulfan**) **55-98-1**; (**interferon** beta serine) 90598-63-3

L126 ANSWER 7 OF 10 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
AN 2003047718 EMBASE
TI Treatment of refractory autoimmune diseases with ablative immunotherapy using monoclonal antibodies and/or high dose chemotherapy with hematopoietic stem cell support.
AU Cohen Y.; Polliak A.; Nagler A.
CS A. Nagler, Bone Marrow Transplantation Dept., Chaim Sheba Medical Center, Tel Hashomer, Ramat-Gan 52621, Israel. a.nagler@sheba.health.gov.il
SO Current Pharmaceutical Design, (2003) Vol. 9, No. 3, pp. 279-288. .
Refs: 134
ISSN: 1381-6128 CODEN: CPDEFP
CY Netherlands
DT Journal; General Review
FS 025 Hematology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
ED Entered STN: 20030207
Last Updated on STN: 20030207
AB Immunological manipulations are the basis for modern treatments of autoimmune diseases (AID). Targeted immune suppression with lymphopenic based chemotherapy, and monoclonal anti B or T lymphocytic antibodies, are integral part of the conditioning for stem cell transplantation (SCT). Immune manipulation by Cyclophosphamide (Cy), ATG, Campath and recently rituximab (RI), with or without stem cell support are the basis for emerging therapeutic modalities aiming to eradicate the autoreactive clone in various autoimmune disorders. Couple of hundreds of SCTs have been recently performed in various autoimmune disorders, mainly **multiple sclerosis** (MS), progressive systemic sclerosis (PSS), systemic lupus erythematosis (SLE) and rheumatoid arthritis (RA). Preliminary results are encouraging. Better selection of patients and earlier treatment, before irreversible organ failure develops will probably improve results. Current ongoing multicenter studies are evaluating the role of SCT in MS, RA, SLE, and PSS.
CT Medical Descriptors:
*autoimmune disease: DR, drug resistance
*autoimmune disease: DT, drug therapy
*autoimmune disease: RT, radiotherapy

*autoimmune disease: SU, surgery
*autoimmune disease: TH, therapy
*hematopoietic stem cell transplantation
drug megadose
immunosuppressive treatment
lymphocytopenia
B lymphocyte
T lymphocyte
molecular cloning
multiple sclerosis: DT, drug therapy
multiple sclerosis: RT, radiotherapy
multiple sclerosis: TH, therapy
progressive systemic sclerosis: DR, drug resistance
progressive systemic sclerosis: DT, drug therapy
progressive systemic sclerosis: TH, therapy
systemic lupus erythematosus: DR, drug resistance
systemic lupus erythematosus: DT, drug therapy
systemic lupus erythematosus: SU, surgery
systemic lupus erythematosus: TH, therapy
rheumatoid arthritis: DT, drug therapy
rheumatoid arthritis: TH, therapy
patient selection
treatment outcome
drug targeting
whole body radiation
drug mechanism
graft versus host reaction: CO, complication
neutropenia: SI, side effect
hemolytic anemia: DT, drug therapy
hemolytic anemia: TH, therapy
pure red cell anemia: DT, drug therapy
pure red cell anemia: TH, therapy
idiopathic thrombocytopenic purpura: DR, drug resistance
idiopathic thrombocytopenic purpura: DT, drug therapy
idiopathic thrombocytopenic purpura: SU, surgery
idiopathic thrombocytopenic purpura: TH, therapy
autoimmune hemolytic anemia: DT, drug therapy
autoimmune hemolytic anemia: TH, therapy
stem cell transplantation
allogeneic stem cell transplantation
disease exacerbation: CO, complication
disease exacerbation: DT, drug therapy
disease exacerbation: PC, prevention
Guillain Barre syndrome: DT, drug therapy
Guillain Barre syndrome: TH, therapy
antiphospholipid syndrome: DR, drug resistance
antiphospholipid syndrome: DT, drug therapy
antiphospholipid syndrome: TH, therapy
enteritis: DT, drug therapy
enteritis: TH, therapy
Wegener granulomatosis: DT, drug therapy
Wegener granulomatosis: TH, therapy
psoriasis: DT, drug therapy
psoriasis: TH, therapy
human
clinical trial
multicenter study
review
priority journal
Drug Descriptors:

*monoclonal antibody: CT, clinical trial
*monoclonal antibody: CB, drug combination
*monoclonal antibody: DT, drug therapy
*monoclonal antibody: PD, pharmacology
*CD4 antibody: DT, drug therapy
*antineoplastic agent: AE, adverse drug reaction
*antineoplastic agent: CT, clinical trial
*antineoplastic agent: CB, drug combination
*antineoplastic agent: DO, drug dose
*antineoplastic agent: DT, drug therapy
B lymphocyte antibody: CB, drug combination
B lymphocyte antibody: DT, drug therapy
B lymphocyte antibody: PD, pharmacology
T lymphocyte antibody: CB, drug combination
T lymphocyte antibody: DT, drug therapy
T lymphocyte antibody: PD, pharmacology
cyclophosphamide: AE, adverse drug reaction
cyclophosphamide: CT, clinical trial
cyclophosphamide: CB, drug combination
cyclophosphamide: DO, drug dose
cyclophosphamide: DT, drug therapy
thymocyte antibody: CT, clinical trial
thymocyte antibody: CB, drug combination
thymocyte antibody: DT, drug therapy
alemtuzumab: CB, drug combination
alemtuzumab: DT, drug therapy
alemtuzumab: PD, pharmacology
rituximab: CB, drug combination
rituximab: DT, drug therapy
busulfan: CT, clinical trial
busulfan: CB, drug combination
busulfan: DO, drug dose
busulfan: DT, drug therapy
thiotepa: CB, drug combination
thiotepa: DO, drug dose
thiotepa: DT, drug therapy
carmustine: CT, clinical trial
carmustine: CB, drug combination
carmustine: DO, drug dose
carmustine: DT, drug therapy
etoposide: CT, clinical trial
etoposide: CB, drug combination
etoposide: DO, drug dose
etoposide: DT, drug therapy
cytarabine: CT, clinical trial
cytarabine: CB, drug combination
cytarabine: DO, drug dose
cytarabine: DT, drug therapy
melphalan: CT, clinical trial
melphalan: CB, drug combination
melphalan: DO, drug dose
melphalan: DT, drug therapy
granulocyte colony stimulating factor: AE, adverse drug reaction
granulocyte colony stimulating factor: CT, clinical trial
CT Drug Descriptors:
granulocyte colony stimulating factor: CB, drug combination
granulocyte colony stimulating factor: DT, drug therapy
granulocyte colony stimulating factor: PD, pharmacology
corticosteroid: CB, drug combination
corticosteroid: DT, drug therapy

immunosuppressive agent: AE, adverse drug reaction
immunosuppressive agent: CT, clinical trial
immunosuppressive agent: CB, drug combination
immunosuppressive agent: DT, drug therapy
azathioprine: CB, drug combination
azathioprine: DT, drug therapy
rhesus D antibody: DT, drug therapy
fludarabine: CB, drug combination
fludarabine: DT, drug therapy
beta interferon: DT, drug therapy
glatiramer: DT, drug therapy
methylprednisolone: DT, drug therapy
prednisone: DT, drug therapy
methotrexate: DT, drug therapy
immunoglobulin: DT, drug therapy
immunoglobulin: IV, intravenous drug administration
penicillamine: DT, drug therapy
interferon: DT, drug therapy
unindexed drug
unclassified drug

RN (cyclophosphamide) 50-18-0; (alemtuzumab) 216503-57-0; (rituximab) 174722-31-7; (**busulfan**) **55-98-1**; (thiotepa) 52-24-4; (carmustine) 154-93-8; (etoposide) 33419-42-0; (cytarabine) 147-94-4, 69-74-9; (melphalan) 148-82-3; (azathioprine) 446-86-6; (fludarabine) 21679-14-1; (glatiramer) **147245-92-9, 28704-27-0**; (methylprednisolone) 6923-42-8, 83-43-2; (prednisone) 53-03-2; (methotrexate) 15475-56-6, 59-05-2, 7413-34-5; (immunoglobulin) 9007-83-4; (penicillamine) 2219-30-9, 52-67-5

L126 ANSWER 8 OF 10 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
AN 2002334081 EMBASE
TI Conference synopsis: Hematopoietic stem cell therapy in autoimmune diseases, October 2001.
AU Openshaw H.
CS Dr. H. Openshaw, City Hope National Medical Center, 1500 Duarte Road, Duarte, CA 91010, United States. hopenshaw@coh.org
SO Biology of Blood and Marrow Transplantation, (2002) Vol. 8, No. 8, pp. 407-411. .
Refs: 12
ISSN: 1083-8791 CODEN: BBMTF6
CY United States
DT Journal; General Review
FS 017 Public Health, Social Medicine and Epidemiology
025 Hematology
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
ED Entered STN: 20021003
Last Updated on STN: 20021003
AB Since 1996, patients with autoimmune diseases have been treated on single-arm investigational protocols with high-dose immunosuppressive therapy and autologous peripheral blood stem cell transplantation (HSCT). In a conference held in October 2001 at the City of Hope National Medical Center, participants discussed current laboratory studies in autoimmunity, the rationale of HSCT in autoimmune diseases, results of phase I-II studies, and the prospects for controlled trials. This conference

synopsis summarizes major discussion points in clinical sessions and in sessions devoted to ethical and regulatory aspects of this investigational treatment. Protocols for controlled studies in **multiple sclerosis** (MS) and systemic sclerosis (SSc), originating in Europe and in the United States, have been designed or are in the final stages of design. The only controlled trial presently underway is for SSc in Europe (Autologous Stem Cell Transplantation International Scleroderma Trial [ASTIS]). There are current plans for a controlled trial for rheumatoid arthritis (RA) in Europe (ASTIRA) but not in the United States. Eventual cross-study analysis of the European and United States trials may give valuable comparative information on the different mobilization and immunosuppressive regimens used. Recognition of the importance of axonal degeneration in secondary progressive MS and the use of mitoxantrone as a rescue medication are two relatively recent developments now being considered in the design of controlled HSCT protocols in MS. The importance of informed consent and study accessibility was discussed as well as the continuing role of the US Food and Drug Administration in regulating these protocols in the United States.

CT Medical Descriptors:
*autoimmune disease: DT, drug therapy
*autoimmune disease: RT, radiotherapy
*autoimmune disease: TH, therapy
*hematopoietic stem cell transplantation
*autologous hematopoietic stem cell transplantation
clinical protocol
drug megadose
autoimmunity
medical ethics
multiple sclerosis: DT, drug therapy
multiple sclerosis: RT, radiotherapy
multiple sclerosis: TH, therapy
systemic sclerosis: DT, drug therapy
systemic sclerosis: RT, radiotherapy
systemic sclerosis: TH, therapy
Europe
United States
rheumatoid arthritis: TH, therapy
stem cell mobilization
immunosuppressive treatment
nerve fiber degeneration
informed consent
health care access
food and drug administration
whole body radiation
cardiotoxicity: SI, side effect
juvenile rheumatoid arthritis: DT, drug therapy
juvenile rheumatoid arthritis: RT, radiotherapy
juvenile rheumatoid arthritis: TH, therapy
idiopathic disease: DT, drug therapy
idiopathic disease: RT, radiotherapy
idiopathic disease: TH, therapy
lymphocytopenia: CO, complication
superinfection: CO, complication
human
clinical trial
phase 1 clinical trial
phase 2 clinical trial
randomized controlled trial
controlled study
review

Drug Descriptors:
immunosuppressive agent: CT, clinical trial
immunosuppressive agent: CB, drug combination
immunosuppressive agent: CM, drug comparison
immunosuppressive agent: DO, drug dose
immunosuppressive agent: DT, drug therapy
mitoxantrone: AE, adverse drug reaction
mitoxantrone: DT, drug therapy
granulocyte colony stimulating factor: CT, clinical trial
granulocyte colony stimulating factor: CB, drug combination
granulocyte colony stimulating factor: CM, drug comparison
granulocyte colony stimulating factor: DT, drug therapy
cyclophosphamide: CT, clinical trial
cyclophosphamide: CB, drug combination
cyclophosphamide: CM, drug comparison
cyclophosphamide: DT, drug therapy
carmustine: CT, clinical trial
carmustine: CB, drug combination
carmustine: CM, drug comparison
carmustine: DT, drug therapy
etoposide: CT, clinical trial
etoposide: CB, drug combination
etoposide: CM, drug comparison
etoposide: DT, drug therapy
cytarabine: CT, clinical trial
cytarabine: CB, drug combination
cytarabine: CM, drug comparison
cytarabine: DT, drug therapy
melphalan: CT, clinical trial
melphalan: CB, drug combination
melphalan: CM, drug comparison
melphalan: DT, drug therapy
thymocyte antibody: CT, clinical trial
thymocyte antibody: CB, drug combination
thymocyte antibody: CM, drug comparison
thymocyte antibody: DT, drug therapy
prednisone: CT, clinical trial
prednisone: CB, drug combination
prednisone: CM, drug comparison
prednisone: DT, drug therapy
busulfan: CT, clinical trial
busulfan: CB, drug combination
busulfan: DT, drug therapy
beta interferon: DT, drug therapy
glatiramer: DT, drug therapy
antirheumatic agent: CB, drug combination
antirheumatic agent: DT, drug therapy
methotrexate: CB, drug combination
methotrexate: DT, drug therapy
leflunomide: CB, drug combination
leflunomide: DT, drug therapy
tumor necrosis factor alpha antibody: DT, drug therapy

RN (mitoxantrone) 65271-80-9, 70476-82-3; (cyclophosphamide) 50-18-0; (carmustine) 154-93-8; (etoposide) 33419-42-0; (cytarabine) 147-94-4, 69-74-9; (melphalan) 148-82-3; (prednisone) 53-03-2; (**busulfan**) **55-98-1**; (glatiramer) **147245-92-9, 28704-27-0**; (methotrexate) 15475-56-6, 59-05-2, 7413-34-5; (leflunomide) 75706-12-6

L126 ANSWER 9 OF 10 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

AN 2002179666 EMBASE
TI Induction of tolerance in autoimmune diseases by hematopoietic stem cell transplantation: Getting closer to a cure?.
AU Burt R.K.; Slavin S.; Burns W.H.; Marmont A.M.
CS R.K. Burt, Division of Autoimmune Disease, Northwestern University Medical Ctr., Searle Bldg, 320 E Superior, Chicago, IL 60611, United States. rburt@nwu.edu
SO Blood, (1 Feb 2002) Vol. 99, No. 3, pp. 768-784. .
Refs: 358
ISSN: 0006-4971 CODEN: BLOOAW
CY United States
DT Journal; General Review
FS 025 Hematology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English
ED Entered STN: 20020606
Last Updated on STN: 20020606
AB Hematopoietic stem cells (HSCs) are the earliest cells of the immune system, giving rise to B and T lymphocytes, monocytes, tissue macrophages, and dendritic cells. In animal models, adoptive transfer of HSCs, depending on circumstances, may cause, prevent, or cure autoimmune diseases. Clinical trials have reported early remission of otherwise refractory autoimmune disorders after either autologous or allogeneic hematopoietic stem cell transplantation (HSCT). By percentage of transplantations performed, autoimmune diseases are the most rapidly expanding indication for stem cell transplantation. Although numerous editorials or commentaries have been previously published, no prior review has focused on the immunology of transplantation tolerance or development of phase 3 autoimmune HSCT trials. Results from current trials suggest that mobilization of HSCs, conditioning regimen, eligibility and exclusion criteria, toxicity, outcome, source of stem cells, and posttransplantation follow-up need to be disease specific. HSCT-induced remission of an autoimmune disease allows for a prospective analysis of events involved in immune tolerance not available in cross-sectional studies. .COPYRGT. 2002 by The American Society of Hematology.
CT Medical Descriptors:
*autoimmune disease: ET, etiology
*autoimmune disease: SU, surgery
*hematopoietic stem cell transplantation
*immunological tolerance
hematopoietic stem cell
adoptive transfer
remission
autotransplantation
outcomes research
autoimmunity
genetic susceptibility
genotype
animal model
immunization
whole body radiation
mortality
multiple sclerosis: DT, drug therapy
systemic lupus erythematosus: DT, drug therapy
systemic lupus erythematosus: SU, surgery
disease activity
scleroderma: SU, surgery
review

priority journal
Drug Descriptors:
*major histocompatibility antigen
*cyclophosphamide: DT, drug therapy
*thymocyte antibody
*alemtuzumab
*carmustine
*etoposide
cytarabine
melphalan
busulfan
betala interferon: DT, drug therapy
interferon beta serine: DT, drug therapy
glatiramer: DT, drug therapy
RN (cyclophosphamide) 50-18-0; (alemtuzumab) 216503-57-0; (carmustine) 154-93-8; (etoposide) 33419-42-0; (cytarabine) 147-94-4, 69-74-9; (melphalan) 148-82-3; (**busulfan**) **55-98-1**; (**interferon** beta serine) 90598-63-3; (glatiramer) **147245-92-9, 28704-27-0**
CN Avonex; Betaseron; **Copaxone**

L126 ANSWER 10 OF 10 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
AN 85101268 EMBASE
DN 1985101268
TI Immunosuppressant treatment in **multiple sclerosis.**
AU Van Den Noort S.
CS Department of Neurology, University of California, Irvine, CA 92717, United States
SO Clinical Neuropharmacology, (1985) Vol. 8, No. 1, pp. 58-63. .
CODEN: CLNEDB
CY United States
DT Journal
FS 037 Drug Literature Index
030 Pharmacology
008 Neurology and Neurosurgery
026 Immunology, Serology and Transplantation
LA English
ED Entered STN: 911210
Last Updated on STN: 911210
CT Medical Descriptors:
*immunosuppressive treatment
***multiple sclerosis**
*drug therapy
clinical trial
drug efficacy
peripheral nervous system
therapy
review
human
central nervous system
blood and hemopoietic system
Drug Descriptors:
*azathioprine
***busulfan**
*chlorambucil
*chlormethine
*cop 1
*corticosteroid
*corticotropin

*cyclophosphamide
*cyclosporin a
*cyproheptadine
*cytarabine
*cytotoxic agent
*gold
*guanosine derivative
*immunoglobulin
***interferon**
*phosphatidylcholine
*levamisole
*lymphocyte antibody
*melphalan
*mercaptopurine
*methotrexate
*penicillamine
*polyinosinic polycytidylic acid
*prednisolone
*prednisone
*snake venom
*thymocyte antibody
*thymosin
*transfer factor

RN (azathioprine) 446-86-6; (**busulfan**) **55-98-1**;
(chlorambucil) 305-03-3; (chlormethine) 51-75-2, 55-86-7, 82905-71-3; (cop
1) **28704-27-0**; (corticotropin) 11136-52-0, 9002-60-2, 9061-27-2;
(cyclophosphamide) 50-18-0; (cyclosporin a) 59865-13-3, 63798-73-2;
(cyproheptadine) 129-03-3, 969-33-5; (cytarabine) 147-94-4, 69-74-9;
(gold) 7440-57-5; (immunoglobulin) 9007-83-4; (phosphatidylcholine)
55128-59-1, 8002-43-5; (levamisole) 14769-73-4, 16595-80-5; (melphalan)
148-82-3; (mercaptopurine) 31441-78-8, 50-44-2, 6112-76-1; (methotrexate)
15475-56-6, 59-05-2, 7413-34-5; (penicillamine) 2219-30-9, 52-67-5;
(polyinosinic polycytidylic acid) 24939-03-5, 26301-44-0; (prednisolone)
50-24-8; (prednisone) 53-03-2; (snake venom) 55230-69-8; (thymosin)
61512-21-8

=> => d his

(FILE 'HOME' ENTERED AT 14:51:39 ON 28 FEB 2006)
DEL HIS

FILE 'HCAPLUS' ENTERED AT 14:51:59 ON 28 FEB 2006
L1 131 S TREOSULPHAN? OR TREOSULFAN?
L2 1619 S BUSULPHAN? OR BUSULFAN?
L3 5 S (DIMETHYL OR DI METHYL OR DIME OR DI ME)()(BUSULPHAN? OR BUSU
L4 6 S DIMETHYLBUSULPHAN? OR DIMETHYLBUSULFAN?
L5 11 S PENTASULPHAN# OR PENTASULFAN#
L6 26 S HEPSULPHAN# OR HEPSULFAN# OR HEPSULPHAM# OR HEPSULFAM#

FILE 'REGISTRY' ENTERED AT 14:56:27 ON 28 FEB 2006
L7 6 S 299-75-2 OR 55-98-1 OR 55-93-6 OR 2374-22-3 OR 13845-24-4 OR
L8 5 S L7 NOT 13845-24-4
E C6H14O8S2/MF
L9 9 S E3 AND BUTANETETROL
SEL RN 1-4
L10 5 S L9 NOT E1-E4
L11 9 S L8,L10
SEL RN
L12 16 S E5-E13/CRN

```
     FILE 'HCAPLUS' ENTERED AT 15:01:25 ON 28 FEB 2006
L13        2114 S L11
L14           3 S THREOSULPHAN? OR THREOSULFAN?
L15        1732 S L1-L6,L14
L16        2430 S L13,L15
L17       14153 S MULTIPLE SCLERO?
                E MULTIPLE SCLEROSIS/CT
L18       11090 S E3-E7
                E E3+ALL
L19       11087 S E3
L20       14197 S E3,E4,E5/BI
L21          26 S L16 AND L17-L20
L22           1 S US20060041015/PN OR (US2005-524144# OR WO2003-EP8957 OR DE200
                E SASS G/AU
L23          15 S E3,E9
L24           4 S L22,L23 AND L16
L25           1 S L24 AND L21
L26           3 S L24 NOT L25

     FILE 'REGISTRY' ENTERED AT 15:06:22 ON 28 FEB 2006
L27           1 S 147245-92-9
L28           3 S (L-ALANINE OR D-ALANINE OR DL-ALANINE)/CN
L29           3 S (L-LYSINE OR D-LYSINE OR DL-LYSINE)/CN
L30           3 S (L-TYROSINE OR D-TYROSINE OR DL-TYROSINE)/CN
L31           3 S (L-GLUTAMIC ACID OR D-GLUTAMIC ACID OR DL-GLUTAMIC ACID)/CN
                SEL RN L28
L32         866 S E1-E3/CRN
                SEL RN L29
L33        2465 S E4-E6/CRN
                SEL RN L30
L34         340 S E7-E9/CRN
                SEL RN L31
L35        1305 S E10-E12/CRN
L36          15 S L32 AND L33 AND L34 AND L35
L37           3 S L36 AND 64-19-7/CRN
L38           3 S C2H4O2 AND L36
L39           3 S L37,L38
L40           2 S L39 NOT C6-C6-C6-C6/ES
L41           2 S L27,L40
L42          12 S L36 NOT L39
L43           8 S L42 AND 4/NC
L44           4 S L42 NOT L43
L45           1 S BRH AND L44
L46          11 S L43,L45,L41

     FILE 'HCAPLUS' ENTERED AT 15:11:36 ON 28 FEB 2006
L47         488 S L46
L48         323 S COPAXON# OR GLATIRAMER ACETATE
L49         542 S L47,L48
L50           4 S L49 AND L16
L51         253 S L16 AND INTERFERON
L52           4 S L50 AND L51
L53           3 S L52 NOT DATABASE
L54           3 S L25,L53
L55          25 S L21 NOT L54
                SEL AN 23
L56           1 S E13-E14
L57           4 S L54,L56 AND L1-L6,L13-L26,L47-L56
                SEL HIT RN
```

```
     FILE 'REGISTRY' ENTERED AT 15:16:10 ON 28 FEB 2006
L58           6 S E15-E20

     FILE 'REGISTRY' ENTERED AT 15:16:21 ON 28 FEB 2006

     FILE 'HCAPLUS' ENTERED AT 15:16:32 ON 28 FEB 2006

     FILE 'WPIX' ENTERED AT 15:18:18 ON 28 FEB 2006
L59           1 S L22
                E R08220+ALL/DCN
L60         334 S E1
                E  RA1QEQ+ALL/DCN
L61          22 S E3-E8
                E RA0CGY+ALL/DCN
L62           6 S E3-E8
                E RADKP3+ALL/DCN
L63           1 S E3-E6
                E R08586+ALL/DCN
L64           2 S E1
L65           6 S (R08220 OR RA1QEQ OR RA0CGY OR RADKP3 OR R08586)/SDCN
L66         325 S (89522-0-0-0 OR 109265-0-0-0 OR 93334-0-0-0 OR 187150-0-0-0 O
L67         389 S L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L14
L68         426 S L61-L64,L66,L67
L69          40 S L68 AND (MULTIPLE SCLERO? OR L20)
L70          45 S L68 AND P517/M0,M1,M2,M3,M4,M5,M6
L71          30 S L68 AND A61P025/IPC
L72          34 S L68 AND (B14-S01 OR C14-S01 OR B12-E01 OR C12-E01)/MC
L73          70 S L69-L72
L74          80 S L48
                E GLATIRAMER/CN
L75           1 S E4,E5
L76          68 S RA1PPM/DCN OR 91565-0-0-0/DCRE
L77           1 S L73 AND L74,L76
L78           2 S L68 AND L74,L76
L79           2 S L77,L78 AND INTERFERON
L80           1 S L79 NOT MATRIX
L81           1 S L59 AND L68
L82           1 S L81 AND L73
L83           0 S L81 AND L74,L76
L84           1 S L81 AND INTERFERON
L85           2 S L80-L82,L84
L86          61 S GLATRIAMER ACETATE OR GLATIRAMER ACETATE
L87           3 S L86 AND L68
L88           3 S L87 AND INTERFERON
L89           3 S L88,L85
L90           2 S L89 NOT MATRICE
L91          68 S L73 NOT L90

     FILE 'WPIX' ENTERED AT 15:30:44 ON 28 FEB 2006

     FILE 'MEDLINE' ENTERED AT 15:31:16 ON 28 FEB 2006
L92        3011 S L11
L93        4245 S L1-L6,L14
L94        4245 S L92,L93
                E BUSULFAN/CT
                E E3+ALL
L95         405 S E76/BI OR E71/BI OR E80/BI OR E81/BI OR E82/BI OR E83/BI OR E
L96           6 S 1 4 BUTANEDIOL DIMETHANESULFONATE
L97           0 S N BUTANE 1 3 DI METHYLSULFONATE
```

```
L98           0 S N BUTANE 1 3 DI METHYL SULFONATE
L99        4321 S L92-L96
L100          4 S L99 AND L20
                E MULTIPLE SCLEROSIS/CT
                E E3+ALL
L101          3 S L99 AND E11+NT
L102          4 S L100,L101

     FILE 'MEDLINE' ENTERED AT 15:34:36 ON 28 FEB 2006

     FILE 'EMBASE' ENTERED AT 15:34:43 ON 28 FEB 2006
L103       9342 S L11
L104       9618 S L1-L6,L14
L105       9618 S L103,L104
L106        676 S L95
L107       9642 S L105,L106
L108      28987 S L20
                E MULTIPLE SCLEROSIS/CT
                E MULTIPLE SCLEROSIS?/CT
L109      26665 S MULTIPLE SCLEROSIS?/CT
                E E3+ALL
                E MULTIPLE SCLEROSIS/CT
                E E3+ALL
L110      26664 S E1
L111          0 S (E3 OR E4 OR E5 OR E8)/BI
L112         52 S L107 AND L108-L110
L113          9 S L112 AND L46
L114        656 S L48 OR GLATRIAMER ACETATE OR GLATIRAMER ACETATE
L115          9 S L107 AND L46
L116          3 S L107 AND L114
L117          9 S L115,L116
L118          8 S L117 AND INTERFERON
L119          9 S L117,L118
L120          9 S L119 AND L112
L121          9 S L113,L120
L122          7 S L121 AND PY<=2003
L123          9 S L121,L122
L124         28 S L112 AND PY<=2003 NOT L123
L125          1 S L124 AND L1,L14
L126         10 S L123,L125
L127         27 S L124 NOT L126

     FILE 'EMBASE' ENTERED AT 15:41:38 ON 28 FEB 2006

=>
```